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OVERSIGHT OF FOOD SAFETY, 1983

HEARINGS

BEFORE THE

COMMITTEE ON
LABOR AND HUMAN RESOURCES
UNITED STATES SENATE

NINETY-EIGHTH CONGRESS

FIRST SESSION

TO REVIEW THE NATION'S FOOD SAFETY POLICIES AND LAWS, FOCUSING ON ADVANCES IN FOOD SCIENCE AND TOXICOLOGICAL TESTING, AND ADVANCES IN THE ABILITY TO IDENTIFY TOXICOLOGICAL SUBSTANCES AND OF THE RISK SUCH SUBSTANCES POSE TO HUMANS

JUNE 8, 9, AND 10, 1983

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CONTENTS

CHRONOLOGICAL LIST OF WITNESSES

Wednesday, June 8, 1983

Page
Kennedy, Donald, M.D., president, Stanford University, and former Commissioner of the Food and Drug Administration 24
Goyan, Jere E., Ph. D., dean, school of pharmacy, University of California, and former Commissioner, Food and Drug Administration 46
Robbins, Frederick, M D., president, Institute of Medicine, National Academy of Sciences; read by Dr. Elena Nightingale, scholar in residence, Institute of Medicine 71
Fisher, Kenneth D., Ph. D., director, life sciences research office, Federation of American Societies for Experimental Biology 79

Thursday, June 9, 1983

Labuza, Theodore P., M.D., professor of food technology, department of food science and nutrition, University of Minnesota 111
Newberne, Paul M., M.D., professor of nutritional pathology, Massachusetts Institute of Technology 114
La Du, Bert, M.D., professor of pharmacology, University of Michigan Medical School 123
DeVita, Vincent T., Jr., M.D., Director, National Cancer Institute, Department of Health and Human Services 134
Wogan, Gerald, M.D., chairman, department of nutrition and food science, Massachusetts Institute of Technology 154
Rodericks, Joseph V., Ph. D., principal, Environ Corp., Washington, D.C 158
Omenn, Gilbert S., M.D., dean, school of public health and community medicine, University of Washington 172
Stallones, Reuel A., M.D., dean, school of public health, University of Texas 229

Friday, June 10, 1983

McMillan, C. W., Assistant Secretary for Marketing and Inspection, Department of Agriculture, accompanied by Edward N. Brandt, Jr., Assistant Secretary for Health, Department of Health and Human Services; Arthur H. Hayes, Jr., Commissioner, Food and Drug Administration, Department of Health and Human Services; and Donald L. Houston, Administrator, Food Safety and Inspection Service, Department of Agriculture 238
Foreman, Carol Tucker, president, Foreman Associates, representing the Consumer Federation of America 262
Haas, Ellen, executive director, Public Voice for Food and Health Policy, Washington, D.C 274
Schultz, William B., attorney at law, Public Citizen Litigation Group, Washington, D.C 288
Jacobson, Michael F., Ph. D., executive director, Center for Science in the Public Interest, Washington, D.C 304
Mayer, Arnold, international vice president, United Food and Commercial Workers International Union, Washington, D.C 316
Roberts, Howard R., Ph. D., vice president, science and technology, National Soft Drink Association, Washington, D.C 332
Gardner, Sherwin, vice president, science and technology, Grocery Manufacturers of America, Inc., Washington, D.C 362

Page
Wilmoth, Robert, associate general counsel, Armour & Co., representing the American Meat Institute 373
Ebert, Andrew G., vice president, research, development and quality assurance, Pet Inc., St. Louis, Mo., representing the National Food Processor Association 390
Heckman, Jerome H., general counsel, the Society of the Plastics Industry, Inc., Washington, D.C 426
Jordan, Ritchie, legislative committee member, the National Pork Producers Council, Suffolk, Va 467

STATEMENTS

American Chemical Society, Fred Basolo, president, prepared statement 636
American Feed Manufacturers Association, prepared statement 591
American Frozen Food Institute, Thomas B. House, president, prepared statement 633
American Industrial Health Council, prepared statement 618
American Medical Association, James H. Sammons, M.D., executive vice president, prepared statement 639
American Paper Institute, Michael C. Farrar, vice president, prepared statement 604
American Public Health Association, prepared statement 641
DeVita, Vincent T., Jr., M.D., Director, National Cancer Institute, Department of Health and Human Services 134
  Prepared statement 138
Ebert, Andrew G., vice president, research, development and quality assurance, Pet Inc., St. Louis, Mo., representing the National Food Processor Association 390
  Prepared statement 393
Edwards, Charles C., M.D., president, Scripps Clinic and Research Foundation, prepared statement 18
Epstein, Samuel, M.D., professor of occupational and environmental medicine, school of public health, University of Illinois Medical Center; Philip E. Hartman, Ph. D., professor of biology, the Johns Hopkins University; Thomas Mancuso, M.D., department of occupational medicine, University of Pittsburgh; Joyce McCann, Ph. D., Lawrence Berkeley Laboratory; Franklin E. Mirer, Ph. D., United Auto Workers; and George Wald, Ph. D., department of biology, Harvard University, prepared statement 656
Fisher, Kenneth D., Ph. D., director, life sciences research office, Federation of American Societies for Experimental Biology 79
  Prepared statement 84
Flavor & Extract Manufacturers, prepared statement 596
Flexible Packaging Association, Richard A. Lillquest, president, prepared statement 579
Foreman, Carol Tucker, president, Foreman Associates, representing the Consumer Federation of America 262
  Prepared statement 265
Gardner, Sherwin, vice president, science and technology, Grocery Manufacturers of America, Inc., Washington, D.C 362
  Prepared statement 364
Goyan, Jere E., Ph. D., dean, school of pharmacy, University of California, and former commissioner, Food and Drug Administration 46
  Prepared statement 51
Haas, Ellen, executive director, Public Voice for Food and Health Policy, Washington, D.C 274
  Prepared statement 277
Heckman, Jerome H., general counsel, the Society of the Plastics Industry, Inc., Washington, D.C 426
  Prepared statement 437
Helms, Hon. Jesse, a U.S. Senator from the State of North Carolina, prepared statement 4
Independent Bakers Association, Frank Manno, chairman, prepared statement 601
Jacobson, Michael F., Ph. D., executive director, Center for Science in the Public Interest, Washington, D.C 304
  Prepared statement 307
Jordan, Ritchie, legislative committee member, the National Pork Producers Council, Suffolk, Va 467

Jordan, Ritchie, legislative committee member, the National Pork Producers Council, Suffolk, Va—Continued
Page
  Prepared statement 470
Kennedy, Donald, M.D., president, Stanford University, and former Commissioner of the Food and Drug Administration 24
  Prepared statement 29
Labuza, Theodore P., M.D., professor of food technology, department of food science and nutrition, University of Minnesota 111
La Du, Bert, M.D., professor of pharmacology, University of Michigan Medical School 123
  Prepared statement 127
Mayer, Arnold, international vice president, United Food and Commercial Workers International Union, Washington, D.C 316
  Prepared statement 318
McMillan, C. W., Assistant Secretary for Marketing and Inspection, Department of Agriculture, accompanied by Edward N. Brandt, Jr., Assistant Secretary for Health, Department of Health and Human Services; Arthur H. Hayes, Jr., Commissioner, Food and Drug Administration, Department of Health and Human Services; and Donald L. Houston, Administrator, Food Safety and Inspection Service, Department of Agriculture 238
National Farmers Union, Ruth E. Kobell, legislative assistant, prepared statement 611
National Meat Association, John G. Mohay, president, prepared statement 659
Natural Resources Defense Council, Inc., Dr. A. Karim Ahmed, Judith B. Klotz, M.S., and David A. Wirth, Esq., prepared statement 637
Naylor Dana Institute for Disease Prevention, American Health Foundation, prepared statement 571
Newberne, Paul M., M.D., professor of nutritional pathology, Massachusetts Institute of Technology 114
  Prepared statement 117
O'Connell, Richard T., president, Chocolate Manufacturers Association, prepared statement 504
Omenn, Gilbert S., M.D., dean, school of public health and community medicine, University of Washington 172
  Prepared statement (with attachments) 177
Ritter, Hon. Don, a Representative in Congress from the State of Pennsylvania, prepared statement 499
Roberts, Howard R., Ph. D., vice president, science and technology, National Soft Drink Association, Washington, D.C 332
  Prepared statement 337
Robbins, Frederick, M.D., president, Institute of Medicine, National Academy of Sciences; read by Dr. Elena Nightingale, scholar in residence, Institute of Medicine 71
Rodericks, Joseph V., Ph. D., principal, Environ Corp., Washington, D.C 158
  Prepared statement 162
Schultz, William B., attorney at law, Public Citizen Litigation Group, Washington, D.C 288
  Prepared statement 292
Stallones, Reuel A., M.D., dean, school of public health, University of Texas 229
Thomas, Paul R., M.S., R.D., public health nutritionist, prepared statement 643
United Fresh Fruit & Vegetable Association, J. Patrick Boyle, government affairs counsel, prepared statement 612
Wilmoth, Robert, associate general counsel, Armour & Co., representing the American Meat Institute 373
  Prepared statement 376
Wogan, Gerald, M.D., chairman, department of nutrition and food science, Massachusetts Institute of Technology 154

ADDITIONAL INFORMATION

Articles, publications, etc.:

  Day Bacon Was Declared Poison, The," by Philip J. Hilts, from the Washington Post, April 26, 1981 12
  "Food Safety in Perspective," by H. R. Roberts, from Food Safety, 1981 536
  "Food Safety and Toxicology," by J. Doull, from Food Safety, 1981 549
  Interpretation of the Delaney Clause: Legislative History, FDA Precedents and Current Scientific Knowledge, memorandum from James H. Wallace, Jr., and Timothy S. Hardy to Richard T. O'Connell 507

Page

Articles, publications, etc.—Continued
- "Monsanto An Copolymer Beverage Bottle Story, The" 429

Questions and answers:
- Responses of Frederick Robbins, M.D., president, Institute of Medicine, National Academy of Sciences to questions asked by Senator Hatch........ 76
- Responses of Kenneth D. Fisher, Ph. D., director, life sciences research office, Federation of American Societies for Experimental Biology to questions asked by Senator Hatch 98
- Responses of Gilbert S. Omenn, M.D., dean, school of public health and community medicine, University of Washington to questions asked by Senator Hatch 365
- Responses of Reuel A. Stallones, M.D., dean, school of public health, University of Texas to questions asked by Senator Hatch........ 232
- Responses of Sherwin Gardner, vice president, science and technology, Grocery Manufacturers of America, Inc., to questions asked by:
  - Senator Hatch 371
  - Senator Grassley........ 372
- Responses of Andrew G. Ebert, vice president, research, development and quality assurance, Pet Inc. to questions asked by:
  - Senator Hatch 398
  - Senator Grassley........ 400
- Responses of Jerome H. Heckman, general counsel, Society of the Plastics Industry, Inc., to questions asked by Senator Hatch........ 434
- Responses of Ritchie Jordan, legislative committee member, the National Pork Producers Council to questions asked by:
  - Senator Hatch 479
  - Senator Grassley........ 498

OVERSIGHT OF FOOD SAFETY, 1983

WEDNESDAY, JUNE 8, 1983

U.S. SENATE,
COMMITTEE ON LABOR AND HUMAN RESOURCES,
Washington, D.C.

The committee met, pursuant to notice, at 9:41 a.m., in room SD-430, Senator Orrin Hatch (chairman) presiding.

Present: Senators Hatch, Quayle, and Grassley.

OPENING STATEMENT OF SENATOR HATCH

The CHAIRMAN. The committee will be in order.

We would like to welcome you to this special hearing of the Committee on Labor and Human Resources, the first of 3 days of discussions on the Nation's food safety policies and laws.

The next 3 days will feature an impressive list of distinguished American leaders and scientists knowledgeable about the laws that govern our food supply and the science upon which they are based.

In the wake of this extensive hearing record, my committee colleagues and I hope to have the information necessary to assess the need for legislative reform. We began this bipartisan effort in the 97th Congress and plan to continue our efforts in the 98th.

Food safety has been, and always will be, an important concern for the well-being and the safety of our citizens. This Nation's food supply is the most advanced in the world. For better or for worse, it is also the most regulated. Many countries depend on American scientific capabilities to establish their own domestic food policies, and certainly much has been done to upgrade U.S. public health and food safety policy since an earlier generation was shocked by the revelations of Upton Sinclair. It is now our inherited responsibility to separate effective and appropriate policy from ineffective and inappropriate policy.

The most recent major food safety amendments were passed back in 1958. Since then, the Food and Drug Administration has done a remarkable job in implementing the law, although not without public debate and controversy. In particular, the scientific advancements of the last 20 years have brought new complexities and intricacies to the implementation of our food safety laws.

Notable among these scientific advances has been our analytical ability to detect substances. This capacity has increased many-fold so that we can now measure a substance in parts per trillion. Because of this, we are able to detect trace amounts of potentially carcinogenic substances which are environmentally ubiquitous but impossible to eliminate.

The Department of Health and Human Services, in the late 1970's, stated, "Indeed, a requirement for warnings on all the foods that may contain an inherent carcinogenic ingredient * * * would apply to many, perhaps most, foods in a supermarket."

We have also been testing more substances and are discovering more toxins. And, from what I understand, our knowledge of the carcinogenic process has increased vastly since 1958. It is not as simple as we thought then.

The most dramatic example of current food safety controversy arose in 1977 over saccharin. The Food and Drug Administration, based on scientific evidence that saccharin induced tumors in test animals, announced its intention to ban saccharin from processed food but would continue to make it available for over-the-counter and tabletop use.

Many of you may recall the debate that followed. Congress decided to permit the use of saccharin based on the scientific data available in 1977 and to direct the National Academy of Sciences to study saccharin and the broader issue of food policy. The purpose of the Academy study was to provide Congress the basis for broader examination of the food safety laws. Today's hearing marks the formal beginnings of the debate.

In a historically related episode, the U.S. Department of Agriculture and the Food and Drug Administration announced plans to gradually eliminate the use of nitrites largely because of a study by the Massachusetts Institute of Technology which initially held that nitrites induced cancer in test animals. Subsequent peer review of the study data concluded that the initial findings were incorrect. We hope to learn over the next few days whether legislative changes would have prevented this error or if they could minimize such events in the future.

During the last several years, I have listened to varying and divergent views on the problems with our current law and what actions should be taken to improve it. A number of groups—for instance, the Congressional Office of Technology Assessment, the Food Safety Council, the National Academy of Sciences, consumer groups, and many Members of Congress on both sides of the Hill and both sides of the aisle—have studied, reported, and proposed how the law should be changed.

Some believe the law should not be changed and would encourage the FDA to exercise more creativity in implementing current law. Others believe that the Delaney clause—zero risk of carcinogens—was realistic in 1958 but not now, given the scientific advances since then.

Still others believe that the concept of zero risk should be expanded to include teratogens and mutagens as well as carcinogens. Others desire less burdensome regulation.

Some would encourage that the law be changed to permit more flexibility in exercising judgment based on the latest scientific knowledge available. We may hear other views today.

For my part, I believe there is yet another point which deserves to be aired. Call it our societal values placed on food and food substances or something called plain old commonsense. Are we willing to take mustard off the market because of trace elements of carcinogens? What do we do in the case of saccharin when we have no other suitable available alternative today? If we really permitted no substance with any amount of carcinogens, would we be willing to do without products containing corn and peanuts, because they may contain a carcinogenic substance called aflatoxin? We know that alcohol is a teratogen, an agent which can cause physical or behavioral birth defects. Yet I do not sense that our society is prepared to resurrect prohibition.

This is why we meet today to begin this thorough and complete congressional reexamination of our food safety laws. Past debate on food safety all too frequently has been overladen with rhetoric. I believe that those on either extreme of the policy spectrum may never be satisfied. It is now time to cut through the rhetoric and responsibly discuss these issues.

As Senator Kennedy and I indicated in our press release, we hope to compile a hearing record that addresses advances in food science and toxicological testing and the advances in our ability to identify toxicological substances and to better learn of the risk each substance poses to humans.

We expect to hear testimony on the appropriateness of the definition of "safe" and the Delaney clause under existing law, and whether the law should be amended to permit the consideration of benefits in food safety decisionmaking and to require independent expert review of scientific information. Finally, we will be interested in comments on the adequacy of FDA's legal authority to assure the safety of the food supply.

Today we are indeed honored to have two former Commissioners of the Food and Drug Administration appearing before the committee. They will testify on their experiences in carrying out the existing food safety laws.

We will also hear from representatives of the National Academy of Sciences and the Federation of American Societies for Experimental Biology.

My colleagues on the committee and I are grateful for your acceptance of our invitation to testify here today as part of the historical effort to help our Government assure a safe food supply for its people.

I would like to note that our distinguished colleague, Senator Jesse Helms, who is chairman of the Agriculture Committee, will submit a written statement for the record, so, without objection, that statement will go into the record at this point.

[Statement of Senator Helms follows:]

STATEMENT OF SENATOR JESSE HELMS
BEFORE THE COMMITTEE ON LABOR AND HUMAN RESOURCES
FOOD SAFETY HEARINGS
JUNE 8, 1983

MR. CHAIRMAN, I WOULD LIKE TO TAKE THIS OPPORTUNITY TO APPLAUD YOUR EFFORTS IN PUTTING TOGETHER A FINE PANEL OF WITNESSES FOR THESE HEARINGS. YOU HAVE INCLUDED A WIDE SPECTRUM OF INTEREST AND EXPERTISE IN THE AREA OF FOOD SAFETY: PAST FDA ADMINISTRATORS, WHO CAN SHARE THEIR EXPERIENCE WITH THE FOOD SAFETY REGULATIONS; SCIENTIST WHO CONGRESS MUST LOOK TO FOR ADVICE ON THIS MATTER; INDUSTRY REPRESENTATIVES; AGRICULTURAL PRODUCERS; AND CONSUMER INTEREST GROUPS REPRESENTING THOSE OF US WHO LIVE DAY-IN AND DAY-OUT WITH IMPACT OF FOOD SAFETY LAWS AND REGULATIONS.

MR. CHAIRMAN, AS YOU ARE AWARE, THE COMMITTEE ON AGRICULTURE, NUTRITION, AND FORESTRY HAS JURISDICTION OVER THE FEDERAL MEAT INSPECTION ACT, THE POULTRY PRODUCTS INSPECTION ACT, AND THE EGG PRODUCTS INSPECTION ACT. THEREFORE, THE COMMITTEE MUST REVIEW ANY PROPOSED CHANGES IN FOOD SAFETY LAWS. FOR THIS REASON, THE

Committee is very interested in the testimony being presented in these hearings.

The Committee on Agriculture, Nutrition, and Forestry and the Committee on Labor and Human Resources have struggled with the complex and difficult issues of food safety. A bill, introduced in 97th Congress by you, Mr. Chairman and which I cosponsored, was an effort in addressing the major issues which are still with us today.

I would like to highlight the principal issues that continue to be of concern.

The "Zero Risk" standard has resulted in a continuing problem for the FDA, consumers and the industry alike. Our Nation's scientific achievements have caused us to trip over ourselves when we are called upon to apply a "zero risk" standard for food additives. We are so technically advanced that Congress has put the FDA in an awkward spot, between and rock and a hard place, if you will. The law which Congress continues to require FDA to operate under has lead to inconsistant and unpredicable

REGULATORY DECISIONS. IT IS TIME WE ADDRESS THIS PROBLEM IN A SERIOUS MANNER.

IN APPLYING A STANDARD OF REVIEW FOR FOOD ADDITIVES, WHAT QUESTIONS SHOULD BE ASKED? IS THE FOOD PRODUCT ABSOLUTELY SAFE, OR DOES THIS FOOD PRODUCT POSE AN INSIGNIFICANT RISK TO CONSUMERS WHEN BENEFIT FACTORS ARE SET IN THE BALANCE? IS THIS A FOOD PRODUCT WHICH IS VITAL TO OUR COUNTRY'S FOOD SUPPLY? IS THIS THE TYPE OF FOOD ADDITIVE FOR WHICH THERE ARE NO AVAILABLE SUBSTITUTES? IS THIS THE TYPE OF PRODUCT THAT CONSUMERS DESIRE?

THIS COMMITTEE IS VERY FAMILIAR WITH STATEMENTS THAT MANY FOODS WE ENJOY EVERY DAY ARE POSSIBLE CARCINOGENS. THE LIST IS A MILE LONG INCLUDING APPLES, BROCCOLI, CABBAGE, SPINACH, POTATOES, CARROTS AND STRAWBERRIES. THOUGH THE DELANY CLAUSE WOULD NOT BAN THESE LISTED FOOD PRODUCTS, THIS LIST PROVIDES A REFERENCE POINT FOR BALANCING RISKS AND BENEFITS. WE MUST FORMULATE A SENSIBLE FOOD SAFETY POLICY WHICH WILL PROTECT THE PUBLIC WITHOUT ROBBING THEM OF AN ADEQUATE AND ENJOYABLE FOOD SUPPLY.

MR. CHAIRMAN, THANK YOU FOR ALLOWING ME TO PRESENT THIS STATEMENT. SOME OF THESE POINTS HAVE BEEN REITERATED TIME AND TIME AGAIN. HOWEVER, WE HAVE A DIFFICULT TASK AHEAD OF US, ONCE AGAIN, IN ADDRESSING THESE NEEDED REFORMS.

The **Chairman**. At this time we will turn to Senator Quayle of Indiana.

OPENING STATEMENT OF SENATOR QUAYLE

Senator **Quayle**. Thank you very much, Mr. Chairman.

I first want to commend you for your leadership in calling these very important hearings on the subject of food safety.

The experience in the past two decades has certainly shown that the complexity of the question surrounding food safety is tinged a bit with controversy. All too frequently, the controversy has deteriorated at times to passion and, quite frankly, ill-informed rhetoric.

I believe all of us would agree that the issues we are to discuss are too important to the well-being of the people we are entrusted to represent to permit a repeat of the counterproductive and the scientifically unfounded debates we have seen in the recent past.

Mr. Chairman, I believe that the careful groundwork and the rigorous objectivity that have gone into these hearings is a welcome change from the recent history of the food safety debate. Hopefully, this will result in constructive responses from us. I believe that you and the ranking minority member are to be commended for setting a good fundamental groundwork to pursue this in an objective manner——

The **Chairman**. I thank the Senator.

Senator **Quayle** [continuing]. So that we can get the facts and information and try to make the best decision.

I believe that we would all agree that there is one underlying reason for these hearings over the next 3 days: the tremendous increase in our knowledge of the food chain and our ability to analyze the various components of our food safety. Such vast enhancement of our knowledge and analytical tools as we have seen over the past 25 years is both a blessing and a curse—a blessing, since any increase in knowledge can aid us in overcoming age-old problems; and a curse, since this knowledge often reinforces deep-seated fears that the enemies of human biology are pervasive and persistent.

The increase in knowledge has led many to believe that our existing food safety laws are outmoded and badly unsuited to the current state of our scientific understanding. The clearest example of this realization is our discovery that many naturally occurring substances in such widely used foods as strawberries, spinach, mustard, and pepper may cause cancer. But we cannot avoid the responsibility such knowledge carries with it.

So we must also recognize that the discovery of small traces of potentially harmful substances cannot paralyze our ability to make rational determinations of the risks that we are willing to incur while still maintaining the integrity of our food safety laws.

The increase in knowledge has, unfortunately, placed us in the inconsistent position of tolerating some potentially harmful substances while banning others. To avoid this dilemma, we sometimes, as a realistic necessity, simply avoid applying the letter of the law.

At the very least, Mr. Chairman, I believe we should attempt to correct such anomalies that we find in the law and the administration of the law.

Over the past 75 years, the FDA has been successful in carrying out its mandate. As a result, the American people have enjoyed great confidence in the safety of our food supply, a confidence maintained through the overall integrity of the food producing and processing industries.

We must retain that confidence, and I believe that we will retain that confidence, and these hearings will certainly add to that.

The hearings we are starting today also take into consideration the understandable concern on the part of members of the food industry that the law take cognizance of the problems caused by existing law and the way it must be administered.

Equally relevant are the warnings from consumer representatives that nothing be done which adversely affects our health and safety, since, after all, we are all consumers of the bountiful food products available to us throughout the year in food markets in every city and town in this Nation.

Quite properly, the FDA looks to Congress for leadership in clarifying points of conflict or discrepancy in current law and for clearly stating the intent of the law so that the agency can act with discretion but with the knowledge that its policies are consistent with the intent of Congress.

Similarly, Congress should not be required to exercise judgment in complex scientific matters where, as is commonly the case, the scientists themselves have legitimate differences over the interpretation and validity of the data. This should not be surprising, since what scientists call fact is really only statistical certainty.

Nevertheless, it is the responsibility of Congress to make the policy decisions and to give clear direction to the agencies of Government when even the level of scientific certainty may be changing. Previous national concern with saccharin, cyclamates, and nitrites in our food supply has only foreshadowed future critical attention to substances like BHA and BHT.

But Congress should not be called upon to decide, in each and every case, if there is a risk of cancer.

I look forward to these hearings, Mr. Chairman, and again commend you for your leadership in this. Basically, the questions that I will be asking, particularly of our two former Commissioners, which I am delighted to have, are, Should we be changing the law, and if so, how? I would like some specific recommendations. This is a general theme that I will certainly be pursuing with the panelists with great interest, Mr. Chairman, I commend your leadership in this area.

The CHAIRMAN. Thank you, Senator Quayle.

Senator Grassley.

OPENING STATEMENT OF SENATOR GRASSLEY

Senator GRASSLEY. Thank you, Mr. Chairman.

I want to say, too, that I am pleased that the committee has scheduled these food safety hearings on food safety regulation and whether the pertinent laws are still adequate and appropriate in view of advancements in science.

As a representative of a State that depends heavily on agriculture, I have long been keenly interested in the issue of food safety and consequently have taken an active role in debates similar to what is ensuing here in the next 3 days.

I appreciate the opportunity afforded by my membership on this committee to further my study and involvement in this area of great importance to consumers, producers, and processors.

Sometimes overlooked in this debate is the fact that farmers and processors are consumers. Since these agricultural interests are most apt to consume a larger percentage of the benefits of their labor than the general public, there exists a strong desire to make certain that their food supply is safe for these individuals as well. In short, the farmer or processor wants to be the first to know if there is a problem with his product.

It is unfortunate, therefore, that food safety debates are too often depicted and perceived as a battle pitting consumers against food processors and producers. This is simply not the case. A safe food supply obviously is in the best interest of everyone.

As it stands, Americans are fortunate in that they enjoy the safest and most wholesome food supply in the world. No one can realistically contend otherwise. Our food safety laws are important factors in achieving this high standard for the American society.

While our Nation's food safety laws have effectively protected American consumers for decades, events in recent years have shown that these laws have not kept pace with modern science and technology. As a result, they have, on a number of occasions, come very close to mandating the immediate ban of safe food substances that offer consumers important and desirable benefits.

Our current food safety laws embody a zero-risk standard of safety, a standard that completely ignores a level of risk and the benefit of a particular substance. Clearly, this standard is unattainable. Furthermore, it is highly impractical, in view of the fact that scientists are able to detect the presence of substances in food in such minute amounts never dreamed of when our present food safety laws were implemented decades ago.

Our food safety regulators are barred from distinguishing from risk, so that they can focus their resources and attention upon those risks that present a real potential for harm to human safety.

Current laws require regulatory action against food substances no matter how insignificant the risk to human health. Any study showing a substance causes cancer is grounds for banning that substance, regardless of whether or not the results of those studies can be extrapolated to the health of humans or have any relevance in making an assessment of risk to humans.

Another serious flaw in our present current law is that Federal agencies are not required to subject food safety studies to the review of scientific experts independent of the regulatory agency involved; in fact, our laws effectively discourage this type of critical review.

Furthermore, current law does not allow an agency to gradually eliminate a substance from foods shown to present safety problems but instead forces an immediate ban regardless of the devastating impact to society that this abrupt action could cause. This can be extremely disruptive to the food supply, particularly in instances where a supply has been used safely for years and for which no substitute exists.

The nitrite fiasco of the late 1970's serves as a good case study which underscores the need for food safety law revision. At that time, when I was a member of the House Agriculture Committee, the Food and Drug Administration and the Department of Agriculture were preparing legislative and regulatory steps to ban the use of nitrites in the processing of meat.

Shortly after these efforts began, I learned that the study upon which these agencies were basing their actions was less than conclusive. These developments concerned me because, of course, consumer protection must be based upon the most complete information available. It must be based upon objective facts, not conjecture.

Two points were of particular concern: First, whether consumers were about to be exposed unnecessarily to meats that could cause death from botulism; and, second, was an unnecessary cloud of uncertainty being drawn over meat products processed with nitrites?

I joined several of my colleagues in urging the agencies to reexamine their findings and their conclusions. I also asked scientists at Iowa State University to organize a study to review the primary data used by the Government agencies in formulating their policies vis-a-vis nitrites. The group went to work immediately, and their conclusions indicated that the evidence did not support the pending actions proposed by FDA and USDA.

In addition, Congressman Wampler asked the Library of Congress to examine all the material, including internal memos, that related to this controversy. Their findings revealed serious shortcomings; for example, that there was essentially no peer review of the study used by the agencies. Anyone interested in reading this report will discover how Government agencies should not go about making decisions banning certain products.

I also requested the General Accounting Office to look into this matter. Their report basically agreed with the findings of the other groups that I have already mentioned. The GAO found that the decisionmaking process of the agencies was poorly executed and that the conclusions of the nitrite study did not warrant the action contemplated.

The basis for the proposed ban on nitrites was once again refuted by a study conducted by the National Academy of Sciences. In December of 1981, the Academy reported, and I quote, "that evidence does not indicate that nitrite acts directly as a carcinogen in animals," unquote. This report brought welcome news to consumers. It also substantiated the fact that producers and processors of meat products have been unnecessarily harmed by inappropriate Government action in implementing food safety laws.

I would like to include for the record at this point, Mr. Chairman, an article by Philip J. Hills which was carried in the Washington Post Magazine on April 26, 1981. This article is entitled, "The Day Bacon Was Declared Poison," and it provides an excellent account of the nitrite fiasco.

The **Chairman**. Without objection, we will place that in the record at this point.

[Material supplied follows:]

The Day Bacon Was Declared Poison

HOW ONE REGULATORY AGENCY, WITH THE BEST OF INTENTIONS, MESSED UP SPECTACULARLY, THREATENING TO CONDEMN A TENTH OF THE AMERICAN FOOD SUPPLY, AND WHY IT COULD ALL HAPPEN AGAIN

BY PHILIP J. HILTS

Nine billion pounds of meat, tons of fowl, fish, cheese and even pet food—on one day in August of 1978 all of it became suspected poison. Ten percent of the entire food supply of America.

Sodium nitrite—the salt that is used to preserve, color and flavor our foods—apparently causes cancer, two regulatory agencies announced jointly on that day.

Nitrite soon became both famous and feared. The hot dog, symbol of the casual American diet, seemed suddenly tainted, colored with disease. And not any disease, but the disease that is unpredictable, lingering, disfiguring and extremely painful. Cancer, according to public opinion polls, is something Americans fear more than war.

Then, one day last fall, with what seemed to be equal suddenness, the regulatory agencies jointly said, "Never mind." It was almost two years to the day after their warnings that the regulators said they couldn't prove that nitrite causes cancer after all. "I had a hot dog for lunch," crowed the commissioner of the Food and Drug Administration.

What happened with nitrites is a classic story of the combat between public and private interests, between difficult science and irascible politics. It is a struggle the regulator—no matter what his political affiliation—must face daily: Decisions must be based on science, which is always slow and often ambiguous, despite the pressures of Washington politics, which are quick, clear and powerful.

That is a volatile mixture. If the regulator goes slowly, as the scientific results are checked and rechecked to assure accuracy, he can be accused of covering up what he already thinks he knows,

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By Karen [illegible]

of being a tool of the business interests he is supposed to regulate, of fiddling while the public burns. If he moves too quickly, he can be accused of recklessly toying with people's jobs, of needlessly damaging industry and the economy, of becoming that government shibboleth—the Washington regulator run amok.

One incident in the nitrite episode expressed the dilemma well. Donald Kennedy, then head of the Food and Drug Administration, wrote in defense of his move to ban nitrites gradually: "Scientific peer review tries to establish the validity of a test . . . It is not a complete guarantee of being right . . . [but] regulators can and must be willing to proceed with less than this guarantee. When serious health risks are involved, scientific evidence suggestive of these risks should be enough to justify regulatory action."

(Someone in the meat industry got hold of this internal working paper and marked in the margin: "BIG MISTAKE!")

Later in the same document, Kennedy concludes, "There are special reasons why we should [run risks of this sort] when the public health is at stake. You have a politically expendable regulator [Kennedy himself] who is prepared to take the blame and will do so if the outcome proves more disastrous than this argument predicts."

At the beginning of the nitrite case, when Kennedy realized how difficult regulation of this simple salt would be, he told his colleagues that this case would be the real, best test of them as regulators.

The test may have been too hard. The result appeared to outsiders to be a series of chaotic charges, and then retreat in disarray.

The small laboratory building in Boston, its bricks blackened with age and soot, was the place the whole drama began. On the top floor is the office of Dr. Paul M. Newberne, a mild-looking man with gray hair and an easy manner.

Newberne is a specialist in animal diet and disease at Massachusetts Institute of Technology. From 1976 to 1978, he raised about 2,100 rats in his laboratory, and fed them nitrite in a dozen different ways. He was testing, for the FDA, the proposition that nitrites cause cancer in animals.

By the winter of 1978, the animals were dead—of cancer, of natural causes, or at the hands of researchers anxious to finish up the experiment and get the cells of the last aged stragglers onto microscope slides.

Lab assistants took the tiny organs from the bodies, pickled them in preservative, inked them with blue stain, impressed them in wax, then sliced them 7/1000 of an inch thick. With the features darkened and the tissue now thinner than paper, the animals' cells had become translucent.

Newberne bent over his gray, double-eyepiece microscope and painstakingly began to count. Among the circular globs and granules of the cells were ones that had become elephantine. There were cells stunted and gnarled with disease. He named cell types and made diagnoses out loud as a secretary wrote. It was a long list that was taken down. There were 50,000 slides to see, to recognize, to judge and to diagnose.

What Paul Newberne found surprised him. He did not simply send a report to the FDA. Nor did he even call in a report. He decided he had better carry his news to Washington in person.

Mankind has been curing meats with salts for 10,000 years without benefit of regulatory agencies to guard the public health. There are cave paintings that show meat being cured with sea salt, a good source of nitrite.

But it was not until this century that chemists discovered that the active disinfectant that prevents deadly botulism poisoning is sodium nitrite. We now know that nitrite is virtually everywhere in nature. It is in vegetables in sizable amounts. It is manufactured in human saliva constantly. In fact, our intake of nitrite from cured products is only a small percentage of our total intake of the chemical.

The hazards of nitrite were discovered beginning in 1954 when scientists began to learn that nitrites, under certain conditions, can combine with a variety of chemicals called amines. Together they make nitrosamines, among the most potent cancer-causing agents known to man. Nitrosamines have been found to be carcinogens in 22 species of animals—a deadly superlative among chemicals.

In 1971, the Food and Drug Administration

Dr. Paul M. Newberne: His hotly contested counts of cells gnarled and stunted by disease launched the scare.

contracted with Newberne and a colleague to study nitrosamines. Newberne got the expected deadly result from his animals. But he got something else as well, something far more disturbing. In one control group, rats had been given nitrite alone, with no amines. Newberne expected to see no nitrosamines formed and no cancers following.

But instead, Newberne reported, this group showed a startling number of lymphomas—malignant tumors, cancers of the lymph system.

It was still two years before Newberne would begin his big study of nitrite, using 50,000 slides. This result was only in a side group, an accidental finding, and could not be relied on for scientific accuracy. But still, it was startling.

The findings meant that nitrite itself might be a carcinogen. If that were found to be true, then the whole focus of worry would have to be shifted back one level, from the nitrosamines to the nitrite itself. Worse, food manufacturers were not adding nitrosamines to food, but *were* adding nitrite to billions of pounds of meat, poultry, cheese and fish.

So it was a few dozen rats, and Paul Newberne's diagnosis of their lymphomas, that began the early history of the great nitrite scare. As a result, the FDA pushed Newberne to do a monumentally large study to learn whether nitrites themselves could cause cancer.

Animal studies of cancer had not been done in any numbers until a few years earlier, in the late 1960s. "The diagnoses in those dark ages went unquestioned," said Dr. Robert Squire of The Johns Hopkins University. "Everybody believed everyone else. The Good Laboratory Practices standard [a uniform standard to assure consistent quality in lab work] hadn't been established yet, and no one suspected the kind of irregularities that could occur."

It is a typical irony in this tale of nitrite that the first accidental result now appears to have been misread and mistaken, according to the pathologist who reviewed the old slides for the government.

"If this early study had been looked at the way we look at these things today, there would have been no need for everything that has happened since . . . I found that half the things called lymphomas were not lymphomas. There was nothing there" to set off the alarm on nitrite, said Squire, who reviewed the work for the government.

Gary Flamm, then assistant commissioner of FDA, said: "Of course, Squire may be right. . . We didn't review that study, but if it came in now I certainly think we would review it in some detail. God, yes."

But the FDA didn't review it. Instead, a much larger study was commissioned to look at nitrite alone, to try to prove or disprove that nitrite itself can cause cancer in rats. That study began in 1975.

There were more than a hundred rats in each of 18 groups, each group fed a slightly different way. Some were fed nitrite in their rat chow, some were fed nitrite in their water. Some got large doses, some smaller doses and some none at all. For Newberne, the result was the 50,000 slides to examine every day for months.

Pathology—the examination of tissue to find abnormalities—is notoriously tricky. The pathologist must be familiar with the look of each different sort of tissue as well as the scores of different tumor types, both malignant and benign.

Paul Newberne, a tall man with a soft southern voice, peers into the gray microscope near his desk and says, "If you've got 10 years of experience looking at that under all sorts of conditions, you know whether it is normal or not. You get a sense of how distended the parts are, whether they are irregular or too long for their type, even though only a few of them are actually misshapen."

Newberne started his career 25 years ago as a veterinarian, working for three years in rural Georgia before returning to Auburn University for his Ph.D. in pathology and the beginning of his animal research career. Along the way, Newberne had earned two distinguished fellowships to study animal pathology, and from school he went directly to head a program in nutritional pathology at Auburn.

In the past two decades, he has continued to devote himself to the study of diet and its effect in animal disease.

"This is why we don't all agree on tumors," said Newberne, nodding toward the microscope. What was there looked like the spotted surface of granite. "The tumors show up at such a wide range in their stages of development, and they look different at each stage. The question is whether it has advanced to the stage where it is irreversible, malignant and must be removed before it kills the animal."

By spring of 1978, Newberne had eyed his 50,000 slides of tissue. Seeing the slides one at a time, he had no sense of their pattern; he did not think he had found any special effect. It was only when he tabulated the number of tumors that he began to think he was finding groups of nitrite-fed mice with two to four times more lymphomas.

Newberne was surprised and a little excited. He flew to Washington to meet with Donald Kennedy, then commissioner of the FDA.

"At that meeting we pushed Newberne very hard on a variety of questions," said Kennedy. "I thought he gave a very strong account of himself, and the conclusion at the end of the grilling of a couple of hours was that a report would soon be in the public record as a major indictment of nitrite."

Newberne recalls showing his data, scratched out on a big pad of paper, to a roomful of people. "I said the result was only suggestive and we needed more studies to find out what's going on. That's all I said. I didn't tell them to go ban nitrite. Never."

It was the beginning of May 1978, and the news spread like a shock wave among the small number of people allowed to hear it. Donald Kennedy was upset, according to those who talked with him later. The FDA had just come through a loud, bitter public dispute over the banning of saccharin, the largest public battle the FDA had ever had to face, bigger than the cyclamate case, bigger than the cranberry brouhaha of years past.

Then, up popped an issue much larger and much more complex. From the beginning Kennedy told his colleagues that this case would be their best test as regulators. It was legally complicated because nitrite was governed by several different, competing laws. It was politically scary because there were possibly billions of dollars worth of consequences that would come from any decision. It was a public health nightmare because it was not a simple matter of removing a hazard from the market—the regulators had to balance two hazards. How many fatal cases of botulism or other disease would occur if nitrite were banned as a protector of foods? How many cases of cancer would be caused if it were not banned?

Kennedy called Carol Tucker Foreman, the assistant secretary of agriculture in charge of food quality and con-

By James K.W. Atherton

sumer services. Her activist approach to food and health issues had already earned her the title of "dragon lady" among pork producers of the Midwest. They believed that "whenever she opened her mouth, pork prices dropped," one meat industry spokesman said.

"Apparently it's true," Foreman said, "that whenever the Commodity News Service carried something on the issue of nitrosamines and our department, the pork belly prices fell the limit. There was quite a lot of fear engendered among the farmers. We just don't know how, in a chemical-filled world, not to frighten people from time to time as we deal with these issues."

Foreman had been wrestling for a few years with the problem of the nitrosamines found in bacon. At just about the time Don Kennedy called, she thought she had finally wrestled it to the mat, arriving at a technical compromise with the meat industry.

She answered the phone in her large second-floor office. "I have some very bad news for you," Kennedy told her. He said he had a study showing nitrite could cause cancer directly, never mind the nitrosamines.

"Oh s---," Foreman said, and sank through the same rapid, dismal thoughts that other regulators say they also had when they heard the news. "All this struggle over the nitrosamines, and now this guy comes in and says that nitrites themselves are the bad actors. This was obviously something much bigger, much worse."

Commissioner Kennedy gathered a group of half a dozen top agency officials to decide what must be done. Contrary to the procedure on smaller matters, he did not turn the Newberne study over to his agency's senior scientists. Kennedy knew that the Newberne report contained political dynamite. He also knew that the FDA was a sieve, which constantly leaked to the press. The fewer people who knew of this report, he figured, the more likely his group would be able to work in peace. This would later turn out to be a key mistake.

Aware that scientific review would take place at some point, the Kennedy group simply went to work on the assumption that Newberne was right. Newberne, after all, had a strong reputation. He was believed to be an especially cautious man in his work and what he said about it.

A single thought hung over the first meetings like a pall: Nowhere had man actually faced the problem of preserving meat without salt. The problem was new and on a scale quite beyond the saccharin flap that had so occupied the previous two years. Epidemics of botulism poisoning could hit the nation if nitrite were suddenly banned. And the applicable law—called the Delaney amendment—seemed to demand an outright ban with no phaseout period.

It was May, and the group talked of picnics: families taking luncheon meat or sausage in plastic wrap and sealed containers. The fatal botulin bacteria grows rapidly in the absence of air. The inside of a sausage or a hot dog is a good place for it to breed. They envisioned children carrying their lunch boxes to school, setting them in the sun for a few hours before lunchtime. That evening, some of them might not come home.

"Since we had no experience with the situation, we had no idea what the real risks were, if some other infections might not result as well," said Flamm. "After all, people will do *anything* with a sandwich. They will subject a sandwich to the most incredible conditions—one man will take it to a foundry and set it down in better than a hundred-degree heat, another who drives a refrigerator truck will put it back there and let it freeze before lunchtime," said Flamm.

The problems facing Kennedy's caucus were more than the fear of disease. Since man has used nitrite salts for so long in so many ways, its trail through the law is a tangle.

When Kennedy's caucus sorted it out in 1978, it was clear that the law was very strict: It demanded that when a substance is found harmful or carcinogenic, it must be banned.

The law simply allowed no phase-out, moratorium or other ways of backing into regulation. In the case of nitrite, Kennedy and Foreman knew a public health disaster was possible if botulism and food poisoning were not carefully contained after a ban of nitrite.

Donald Kennedy: His "real, best test" as a regulator dissolved into chaotic charges, then retreat in disarray.

A nitrite ban could lead to economic chaos for the meat industry, which in nitrite-treated red meat alone is a $12.5 billion operation.

By law, the regulators simply could not consider these things. They did anyway.

Kennedy's strategy was to develop a 50-page paper detailing the options ranging from no action at all to an immediate ban, and then choosing the most reasonable course—a phase-out of nitrite based on the speed with which the nation could find substitute ways of preserving meat.

The group found that refrigeration would not work—too few refrigerators, too many that might break down and let the meat temperature rise above the 40-degree safety mark. Luncheon meat, hot dogs and the like would have to be frozen. To do that, the nation's freezer capacity would have to be doubled.

Over the years, about 700 chemicals have been tested to see if any might make acceptable substitutes. Nearly all have been failures.

To get around the rigid law, Kennedy and his group decided to adopt the tactics of their opposition in the saccharin battle. In that one, they were forced to give up their ban when Congress passed a law declaring a moratorium on the issue. Kennedy thought they might bring their own bill to Congress—this time to prevent *themselves* from banning a substance.

Up to this time, Kennedy had not worried about the scientific data. He had sent the Newberne report to reputable scientists around the country for them to review, checking statistics and logic. Of course, they could not check the pathology. The reports came back positive—the paper itself seemed all right.

At that moment, in late June, Kennedy had no idea that the Newberne study would eventually go well beyond the usual peer review that scientific papers get. "There are two kinds of scientific review," Kennedy explained. "One is peer review, in which a paper is passed out to referees to look it over and see if the conclusions can be justified by the data. A pathology review is something entirely different. It is like a new experiment, only it takes as raw material the data of an older experiment. It is costly and time-consuming and you don't conduct one until it becomes clear that there is a problem with the study.

"Early on, it was not apparent to me that a pathology review was necessary. Actually, earliest on, I wouldn't have known a pathology report if it ran over me in the street," Kennedy said.

"What one does as commissioner when you've got issues in half a dozen scientific areas buzzing around you—you just ask the best questions you can, and decide on the basis of the answers what needs to be done."

So he and his small group of officials worked out a compromise among bitterly competing interests. Only later, at the insistence of other scientists at the FDA, was the deeper scientific review started. A little too late to avoid embarrassment, as it turned out.

Outside the closed circle of Kennedy's caucus, those other FDA scientists had been worried. Politics was being discussed and decided, but no science. The senior scientists waited through the summer, but were not consulted and were not given copies of Newberne's study to review.

The action by Kennedy to keep Newberne's study secret even from the senior scientists at the FDA is the decision that has since been most vigorously attacked by critics. It has also been criticized in a General Accounting Office investigation and in a Congressional Research Service report.

After the FDA had Newberne's report for two months, chief scientists at the FDA began to realize that they were being cut out of the decision-making. Whether their judgment was necessary or even useful, they felt hurt to be left out, and upset that their skeptical point of view was not getting a proper hearing. No scientific review was taking place. But political plans were already far along.

"On many an occasion," said Dr. Albert Kolbye, associate science director of the Foods Division of the FDA, "I expressed to Dr. [Howard] Roberts, my immediate superior, my growing dismay and concern that events were proceeding too quickly without an adequate foundation of scientific review. I have never ex-

The Washington Post Magazine/April 26, 1981

perienced before in my government career a situation where the word was [that] most of us were to be excluded and not to get involved."

Flamm, too, worried. "We had been alerted to something that was wrong with the study. Newberne had called in and changed the numbers of rats supposed to have tumors. He changed them not once, but twice, then three times that I heard about. And they all moved the number of tumors downward. This is extraordinary, and it made us very nervous.

"This was an important case," Flamm said. "I was concerned, extremely concerned, that I should do the right thing. . . During that time I began to walk in the woods of West Virginia with my wife to talk about it. I knew that if I screwed up on this, I would leave government work altogether.

"When the Newberne numbers started to change, we told Kennedy that it was serious. Our case might be going straight down the tube."

Then, the scientists heard that Kennedy was likely to hold a press conference soon to announce plans. They heard the news first by rumor and then by reading it in Food and Chemical News, a trade publication. Kolbye barked loudly about this. Before the supposed press conference, Gary Flamm was asked to help anticipate critical questions about the Newberne study.

"I was role-playing. I was supposed to be Giovanni Salami, the head of the Meat Industry of America. I worked over two FDA scientists and criticized the Newberne report. I think I hit it impressively hard," Flamm said.

Kennedy says he was not told of the three successive changes in Newberne's data. If he had been, he says, it would have shocked him into some quick action. But by the time Kennedy turned from the political and legal questions to the scientific ones, it was August.

Suddenly, the bubble of privacy enjoyed at FDA was burst.

Marian Burros, food editor of The Washington Post, called the FDA, saying she knew of the Newberne study and was going to run a story on it. The FDA concluded that a public statement had to be made.

"Nothing was secure at FDA," Kennedy lamented. "I actually had members of Congress getting internal memos before I got them!"

On a Friday, Aug. 11, a joint statement was issued by the FDA and the USDA.

"A study recently completed for FDA by the Massachusetts Institute of Technology strongly suggests that nitrite produces cancer of the lymphatic system in test animals," the statement said.

Within a few days the 50-page document that the Kennedy caucus had been working on was in the hands of the press. The report said: "FDA has received a report from Dr. Paul Newberne of MIT . . . The agency has evaluated the study and has concluded that it shows that nitrite induces cancer when ingested in laboratory rats . . . FDA expects that its conclusion will withstand further analysis . . . Accordingly, FDA and USDA are planning for a phaseout of nitrite over a period of several years."

There was no more time for deliberation. Everyone was in the water now; the free-for-all began.

The loudest squeal came from the pork producers. "Consumerist zeal running roughshod over science and common sense," was one observation. "The meat industry," said a Senate Agriculture Committee report, "especially the pork producers, are convinced that removal of nitrite will result in their economic ruin."

One of the unspoken concerns at the time, but one which may have been a major factor in the thinking of meat industry executives, was mentioned by Paul Newberne: "You have to remember that nitrites let them off the hook on many points. Not just botulism. They can be a lot less sanitary in their plants, and so they can spend a lot less money cleaning up and using special equipment. Nitrite, you know, is an excellent disinfectant. I suspect this thought played an important role."

"A nitrite ban would cause prepared meats to disappear," said a Tennessee newspaper in quoting a meat industry spokesman, "disrupting the food supply. The hog industry would be decimated, since 70 percent of U.S. pork ends up in processed meats. What is more . . . nitrite protects against the poison that causes botulism. Banning nitrite could save, say, 2,000 lives from cancer each year and lose 10,000 to food poisoning."

Consumer activists were not happy either. "Carol Foreman and Donald Kennedy should go back to the law and read it because they are violating it," said Ralph Nader. The Environmental Defense Fund attacked the agencies for "laying low when they should be racing ahead."

Although the consumerists wanted an immediate ban, the industry wanted no ban and no hints of severe action either.

But even as the FDA and the USDA were weaving a defense for their actions on TV and in interviews, FDA scientists were unraveling it from the other end.

Within six weeks of the announcement that would have altered the eating habits of virtually the entire nation, FDA scientists already knew that the Newberne study had problems. In late September, two independent pathologists looked at the slides that were supposed to contain the rat tumors found by Newberne. The two worked separately, but their conclusions were virtually identical.

They disagreed with Newberne on 29 of 35 animals checked. This result was enough to knock the Newberne study below the level of statistical significance, even though only a seventh of the tumorous animals had been checked.

By today's standards, Newberne's diagnoses of that time are considered loose. He lumped together different sorts of tumors under the category of lymphoma.

The FDA soon decided to have all 50,000 slides done by Newberne reviewed by other expert pathologists—a group called the Universities Associated for Research and Education in Pathology (UAREP). Forty-six pathologists looked

Senator **Grassley**. This is the story that the Post described of how one regulatory agency—and I am quoting—"with the best of intentions, messed up spectactularly, threatened a 10th of the American food supply, and why it could happen again," unquote.

It has become increasingly clear that this must not happen again. Congress should not have to apply pressure for adequate peer review as in the nitrite example in order to assure no serious flaws exist in studies from which a ban on food substances could result.

Furthermore, when a substance has long been safely used and has no practical substitute, agencies should be authorized to phase out a substance discovered to be unsafe in instances where consumers are not exposed to unreasonable health risks.

It is important that consumers are not deprived of a beneficial food ingredient and subjected to unnecessary disruption in food supply.

In conclusion, food safety laws do not serve consumers well if Congress has to step in on a case-by-case basis—as an example, the saccharin moratorium just passed by this Congress—in order to carry out the will of the public for a more reasonable, flexible administration of food safety policy.

As it stands, our present laws do not provide this essential flexibility because these laws are not responsive to modern technology and do not allow agency decisionmakers to exercise their best judgment. Our citizens deserve better food safety laws than those which require crisis management by the Federal Government. The time is now for Congress to move ahead with a serious review and revision of food safety laws. Our country cannot afford to wait for another crisis such as with saccharin and nitrites before Congress finally decides to act responsibly in developing a more reasonable, appropriate food safety policy.

Thank you, Mr. Chairman.

The **Chairman**. Thank you, Senator Grassley. We appreciate it.

We will first hear this morning from Dr. Donald Kennedy, who is currently the president of Stanford University and, I might add, in the midst of commencement activities. We really appreciate your presence here today.

Dr. Kennedy, of course, has been on the cutting edge of the food safety debate for many years. Among other pertinent experiences he had while serving as Commissioner, Dr. Kennedy saw both saccharin and nitrites come under public scrutiny and debate.

Following Dr. Kennedy, we will hear from Dr. Jere Goyan, presently serving as dean of the School of Pharmacy at the University of California at San Francisco. Dr. Goyan followed Dr. Kennedy as FDA Commissioner during the Carter administration.

We invited two other FDA Commissioners who, for unavoidable reasons, could not attend: Dr. Charles C. Edwards, president and chief executive officer of the Scripps Clinic and Research Foundation, and Dr. Alexander M. Schmidt, vice chancellor for health affairs at the University of Illinois at Chicago.

Both of these will submit their statements for the printed hearing record, and their statements are, likewise, very important in this overall debate.

[The prepared statement of Dr. Edwards follows:]

Statement of

Charles C. Edwards, M.D.

President of

Scripps Clinic and Research Foundation

La Jolla, California

before the

Committee on Labor and Human Resources

United States Senate

on

Food Safety Policy

June 8, 1983

Mr. Chairman and members of the Committee, my name is Charles C. Edwards. I am President of the Scripps Clinic and Research Foundation in La Jolla, California. From late 1969 to mid-1973, I served as Commissioner of Food and Drugs. For the next two years I served as Assistant Secretary for Health in the Department of HEW, and in that capacity had oversight responsibilities for the work of the Food and Drug Administration.

During my tenure as FDA Commissioner the problems with food safety policy that are so apparent today were just beginning to make themselves known. Three particular controversies that persisted throughout that time, and undoubtedly continue to this day, illustrate those problems.

Nitrites. Twice while I was at FDA, congressional hearings were held to investigate the safety of the use of nitrite in food processing. Charges were made that nitrite was itself dangerous and that it combined with amines to form carcinogenic nitrosamines. It was apparent to me, however, that nitrite was essential to the production of cured meat and that consumer demand for such products as bacon far out weighed whatever theoretical risk might be attributed to nitrite. Accordingly, we took action in 1972 to ban unimportant uses of nitrite but to permit the continued use of this substance "for obtaining the essential characteristics of cured meats."

It is important to note that our action at this time was not based just upon the use of nitrite in preventing botulism. The principal reson we did not ban all nitrite use was because of its importance in maintaining the characteristics of cured meat that are expected and demanded by consumers. The notice published in the Federal Register in November 1972 made this clear:

> "At the present time the use of nitrites and nitrates (insofar as nitrates are converted to nitrites) is essential in the production of certain staple foods in maintaining the characteristics of color, taste, and texture which the consumer through long exposure has come to associate with and demand of such foods. For example, without nitrite bacon is salt pork, frankfurters are bratwurst, and ham is salty roast pork."

These uses of nitrite remain approved today and should, in my judgement, remain approved in the future unless another curing ingredient is developed that produces the same characteristics of color, taste, and texture.

Saccharin. During my tenure at FDA, the safety of saccharin was questioned on two separate occasions. In response to initial findings at the University of Wisconsin in 1971, saccharin was removed from the GRAS list and regulated through an interim food additive regulation. When a further study confirmed bladder cancer in test animals, I requested a report and recommendations by the National Academy of Sciences.

Technically, I could have banned saccharin immediately under the Delaney Clause, in early 1972, on the basis of those animal studies. I did not take that step because, once again, it was clear to me that the law should not be interpreted to yield absurd results. Saccharin was, at that time, the only remaining nonnutritive sweetener on the market. American consumers demand the availability of diet food products. It is irrelevant whether these diet products produce quantifiable health benefits or whether consumers simply like them. The point is that saccharin, like nitrite and many other important food substances, has come to be accepted and expected by the American public, and any law which does not recognize this simply will not work.

Diethylstilbesterol (DES). During my entire time at FDA, there were congressional hearings and public debate about the safety of DES for use as a growth promotant in animal feed and animal implants. We lenghthened the withdrawal period in 1971 to increase the margin of safety but then, in mid-1972, abruptly withdrew DES from the market when it became clear, through more sensitive detection methodology, that any use of DES in food-producing animals would leave some residue of this substance in the food intended for human consumption.

Before the DES episode we had regulated carcinogenic animal drugs under the theory that, if no residue could be detected at 2 parts per billion (ppb), we would simply conclude that it was not there at all or in any event should be of no public health concern. While we now recognize this is an indefensible approach, it was the best we could do at that time.

Out of the DES episode came a much more scientific and justifiable approach -- the use of quantitative risk assessment to determine whether the risk presented by the residue of an animal drug is significant or insignificant. This approach had been agreed to by the time I left FDA, and I am happy to see that in intervening years it has been improved and extended to other food safety decisions.

Quantitative risk assessment is not an accurate predicter of risk, but it does allow FDA to determine the maximum potential risk and thus realistically to distinguish between significant risks that should be regulated and insignificant risks that are of no public health concern. It is apparent to me that, in the years ahead, all food safety decisions, and particularly those involving carcinogens, must rest upon this continually evolving approach. In the years to come it will undoubtedly be improved substantially, as our knowledge of basic biology increases, but I anticipate that the quantification of risk represents the entire future of food safety policy.

These three matters, with which I had to grapple more than ten years ago, did not present simple issues then, do not present simple issues today, and are unlikely to be easily resolved in the near future. They capture the essential dilemma of all food safety problems. We never have had a risk-free food supply, and we never will have one. Thus, future food safety policy must recognize the distinction between significant and insignificant risk and must provide a mechanism for allowing the continued use of some substances which, although presenting a significant risk, are simply too important to our traditional food supply to allow them to be banned.

There is no single or magical way to do this. I have been too far removed from this issue for the past 10 years to suggest any particular form of regulation or statutory language that will accomplish these purposes. I certainly regarded the present statute as sufficiently flexible to avoid taking silly action against important food substances, but Congress may also wish to establish a new statutory mandate.

Whichever way these problems are approached, it is of fundamental importance that FDA retain substantial flexibility and discretion in interpreting and applying food safety policy in this country. Congress cannot anticipate all the issues that will arise, and FDA cannot be expected to hold off decisions indefinitely while new legislation is debated and enacted. The American public looks to FDA for leadership in food safety policy, and the Agency must be in a position to respond immediately to whatever issues arise.

The CHAIRMAN. So I would like to welcome both of you before our committee. We are deeply grateful that you are taking time to help this committee better understand not only the importance of this debate but also the possible solutions and suggestions that might help us to resolve it in an effective and reasonable manner.

Dr. Kennedy, we will turn to you.

STATEMENT OF DONALD KENNEDY, M.D., PRESIDENT, STANFORD UNIVERSITY, AND FORMER COMMISSIONER OF THE FOOD AND DRUG ADMINISTRATION

Dr. KENNEDY. Mr. Chairman, thank you very much. I am really very grateful for the opportunity to appear before you on this very important subject.

I do want to make it clear at the outset that I am not testifying on behalf of any particular set of legislative proposals, nor even for the enactment of statutory changes at this particular time.

I think that both the specific character and the desirable timing of statutory reform are best judged by people who have continuing contact with the issues and with the legislative process on those issues, and as you well know, I don't have either one. But I hope I may play a useful role in these proceedings by citing some of the deficiencies in the FDA's statutory authority that I encountered as Commissioner and by describing some of the recommendations my colleagues and I prepared to improve matters during my tenure as Commissioner.

First, I just want to make, if I may, two rather general points about the process of statutory reform. We are talking about legislation that has a very long history both of periodic amendment and of energetic interpretation through regulation writing.

Under those circumstances, law and the regulations that are based on the law often pass beyond public and even congressional understanding, so that scientifically and legally appropriate actions under the law may sometimes produce a degree of public consternation that embarrasses both the agency and the Congress.

The very process of legislative reform, through education as well as through legal clarification, serves to recalibrate our understandings about the law, about its purposes, and about how those purposes match up to the public's expectations. In the course of statutory revision, complex regulatory provisions can also either be codified or eliminated.

As new problems have arisen over the past quarter century, FDA has attempted to solve some of them, sensibly enough, by promulgating regulations; but the body of regulations has gradually become a thicket of confusion so dense that it doesn't benefit anybody, with the possible exception, Mr. Chairman, of the private food and drug bar in your city.

That description, of course, could fit the difficulties we have with many old laws. What is special about the Food, Drug, and Cosmetic Act is that it deals centrally with matters of science and technology, as you and your colleagues have pointed out in your opening statements.

Not only are science and technology not static; they progress differentially, creating new problems for old understandings. For example, the science of analytical chemistry has developed more rapidly than that of toxicology, so we find ourselves in a position to detect more than we can evaluate and to measure more than we can understand.

So the matters with which I think it is important to deal at some point in a revision of the statute are these, and I put them to you as questions:

First, is the general safety standard of the law appropriate; that is, does it set a reasonable and useful threshold for approval of a food additive?

Does the present law give adequate scope for scientific progress and for improvement of technique?

Should the agency be permitted more discretion in the timing of actions it proposes?

Should there be an opportunity to consider benefits in decisionmaking about food safety?

Should there be some statutory specification of ways to use scientists outside the agency in evaluating the scientific basis for FDA's decisions?

Let me begin with the question of levels of risk. I think the general standards of safety for food additives are wise and that they surely should be retained. They put upon the proponents of use the burden of demonstrating that a substance is safe.

To those basic provisions have been added, in the course of amendment, some more explicit ones, the best known of which—the Delaney clause—embodies a number of scientific assumptions. In prohibiting any amount of a substance that has been shown to induce cancer in man or animals, for example, the Delaney clause states a strong hypothesis about the biological significance of very low doses.

My own view, which I stated on a number of occasions at the end of my time as commissioner, is that the Delaney clause should be made more flexible before it breaks. Let me give an example of the sort of difficulty I have in mind. As a biologist, I find it almost certain that some carcinogenic substances will be shown to behave as though there were a biological threshold for their action.

Similarly, it is likely to emerge that certain species of test animals are inappropriate for demonstrating the human carcinogenicity of certain classes of chemicals because those animal species lack the enzyme systems that, in man, serve to detoxify or inactivate those compounds.

Now, the Delaney clause in the present law provides no incentive whatever to seek out such exceptions and to justify them scientifically. Accordingly, I believe that the language of the Delaney clause should be revised to permit more scientific discretion in deciding whether a substance causes cancer in humans. That could be done by changing the absolute character of its prohibition, so as to permit exceptions if there is a showing that the concentrations to be found or expected contribute no added risk.

A much more difficult question for me is whether the general standard of safety should be changed so as to permit risks that are insignificant, trivial, or negligible—all terms, by the way, Mr. Chairman, that can be found in the various recent efforts to propose modifications in the food safety laws, and all implying the acceptability of some small amount of risk.

I think this is a difficult question to talk about, partly because the language is itself confusing. As a matter of fact, the definition sections of the various recent legislative proposals illustrate exactly the these confusions. I think some of the staff members here are smiling because their own involvement in those efforts has shown them how difficult it is. The current standard is "reasonable certainty of no harm." You will note that that is essentially a probabilistic assertion. It concedes the possibility of error in our judgment about risk, but stops short of suggesting that a small but certain risk would be acceptable.

Efforts to reinterpret or rephrase this concept, it seems to me, ought to be forthright. It is one thing to say that we can accept some small probability that our judgment is incorrect but quite a different thing to say that we are prepared to accept certain risks as long as they are small. The second formulation raises, directly and immediately, the question, "How small is small enough?"

I think it is essential for Congress to face up to this question. For too long, all of the risk statutes—not just FDA's but EPA's and everybody's—have been almost deliberately vague on this point, sending agency heads out with instructions that sound to them a little bit like, "Keep the people safe, but be reasonable about it."

That simply requires the agency head to guess at congressional intent and then to take the heat if the guess turns out to be wrong.

Risk estimation is still, obviously, a poorly understood science, and it adds to all the uncertainties of toxicology the additional difficulty of translating from animal effects to human risks. Nevertheless, useful—even though broad—approximations are possible using risk estimation techniques, and I would think that at least as a part of the legislative history, some approximation of the Congress view of what a negligible risk is should be given; say it is one estimated incremental cancer death, lifetime, per million population. That is a number that has been around, largely because it is included in FDA's sensitivity-of-the-method regulation, and it is a place to start. It is also a risk that would be quite modest with respect to others that could be prevented—but are not prevented—by very modest legislative intervention, like lowering speed limits by a mile an hour or so.

I expect that you will be urged by some to include consideration of benefits as part of the regulatory process for food additives, and it is my hope that you will approach that proposition with some caution.

Both the saccharin and the nitrite cases show that health benefits can enter the consideration of food additive safety in significant ways, but, unfortunately, health benefits is a difficult term to define, and it can be made either so narrow as to be useless or so broad as to be limitless. My own inclination is to recommend that health benefits be defined fairly broadly, but that they be considered only for those additives with a substantial history of use in the food supply and where there is no practical substitute for the already-used additive.

There should also be a stringent requirement that the health benefit be demonstrated, not just shown to be plausible. The Congress ought to require more than hand waving; it ought to require a serious showing.

Arguments will no doubt be made for the extension of risk/benefit comparisons to include economic benefits, and that, I think, is a very slippery slope indeed, and I urge you not to wander far onto it. Risk/benefit balancing can only be carried out successfully in a limited universe where risks and benefits are measured in the same kinds of units. It is difficult enough to compare the health benefits associated with the protection that nitrites provide against botulism with the health risks they may impose, but at least we are talking about the same thing when we talk about the numerator and the denominator in that ratio. Consider how much more difficult it would be if we were asked to weigh the health risks of a food additive against its distributed economic benefits. I think that anybody who is asked to give serious consideration to that proposition ought to ask in return whether the person making it is prepared to state exactly what dollar value he or she places on a single human life. Only if you know that number are you making the agencies accountable for a process or a value that you are willing to define.

We did learn from the nitrite episode that FDA lacks adequate discretionary authority with respect to the timing of bans. You may recall, Mr. Chairman, that in view of the importance of nitrites in providing protection against botulism and the need for technological transition in the industry, FDA and USDA proposed to phase out the use of those food additives over a period of 3 years instead of immediately.

Unfortunately, the Justice Department took a look at that and told us that it had never heard of a dance called the "Slow Delaney," and a reasonable approach to a troublesome problem was ruled out. So I would hope that Congress would consider it reasonable to grant the agency statutory authority for a phaseout, perhaps limited to a few years—three sounds adequate to me for most cases—and restricted to those already existing additives for which there is not a reasonable or practicable substitute.

Last, let me turn to the problem of peer review. The decisions made by a scientific regulatory agency nearly always rest on judgments of probability and not certainty. It is sometimes necessary to decide, even when the data are not as complete or convincing as you would like, that a certain result or set of results produces a reasonable probability of risk.

Some parties are inevitably going to dislike every decision, so there is always room for reinterpretation and recalculation. Understandably, those negatively affected often believe that a system for external peer review would offer an added guarantee against unwise or unfavorable regulatory judgment.

I think perhaps it will—although I think that peoples' expectations about that are quite unrealistic. Those expectations, furthermore, ignore some significant costs of a formal external system of peer review. It extends the opportunity for second guessing, and it may prolong the time it takes to undertake a really needed action. It may also reduce the incentive for good scientists to do their work inside the agency by implying that their judgments are of intrinsically lower worth than those of outsiders.

So I regard the proposal as a mixed blessing, and I urge that it be given a very cautious and skeptical reading by you and your colleagues. I would mainly urge that you not expect too much of it. In fact, FDA did do an informal peer review on the nitrite study and on the regulatory proposals resulting from it. I do not think that a formal process of externally run and mandated peer review would have changed that result in the slightest, because in fact the event that produced a change in that result—at least for now—is a pathologist's review of the slides. No peer review committee is going to do that; peer reviews don't reprocess and redo the primary data, and may barely even redo the statistics.

To construct something that would, in effect, redo the studies would, I think, be hopelessly cumbersome. So peer review may have some utility in the way it is used, for example, in the drugs area by FDA advisory committees. I would urge you to look at that for your model rather than at the proposals that have been on the table in the food area.

The best place to put peer reviews close enough to the agency so that there is an option not to refer relatively unimportant or routine matters, so that the relationship is close enough to insure that matters get referred relatively early in their consideration, and so that the members of the review group can be chosen with FDA participation and subject to the conflict of interest and other provisions that apply to Government advisory committees generally.

Finally, I would urge that you not ignore those parts of the food safety laws that deal with FDA's authority to act. As we make the standards for safety and the procedures of approval of food additives better tuned to modern science, we want at the same time to strengthen the capacity of the Agency to remove unsafe products from the market expeditiously, to conduct inspections, and to trace hazards more effectively.

Mr. Chairman, I hope these thoughts are useful to you. I am very grateful to you and your colleagues for holding thorough hearings on this important subject. There is not a trickier or a more controversial area in which to legislate than the avoidance of public health risks, and the food safety laws are, in a way, our model for dealing with such risks.

After 4 years away from my own responsibilities in this arena, I am still convinced that it is about as important a job as anyone can undertake. You are dealing with a statute that is basically sound. It needs only some tuning to make it conform to contemporary scientific reality.

The agency responsible for administering that statute is also sound and full of able and dedicated people. They deserve the very best tools you can give them to work with. Thank you very much.

[The prepared statement of Dr. Kennedy follows:]

TESTIMONY ON FOOD SAFETY LEGISLATION

FOR:

SENATE COMMITTEE ON LABOR AND HUMAN RESOURCES

JUNE 8, 1983

DONALD KENNEDY, PRESIDENT

STANFORD UNIVERSITY

FORMERLY COMMISSIONER OF THE FOOD AND DRUG ADMINISTRATION

MR. CHAIRMAN AND MEMBERS OF THE COMMITTEE, I AM DONALD KENNEDY, PRESIDENT OF STANFORD UNIVERSITY; FROM APRIL OF 1977 TO JULY OF 1979, I SERVED AS COMMISSIONER OF THE FOOD AND DRUG ADMINISTRATION. FOOD SAFETY WAS IMPORTANT TO ME THEN, AND IT IS IMPORTANT TO ME NOW. THE BODY OF LAW AND REGULATION UNDER WHICH WE PROTECT THE SAFETY OF THE FOOD SUPPLY IS AN IMPORTANT PART OF ANY NATIONAL STRATEGY OF PREVENTIVE HEALTH.

FOR THAT REASON, I AM GRATEFUL FOR THE OPPORTUNITY TO APPEAR BEFORE YOU ON THIS IMPORTANT SUBJECT. BUT I WANT TO MAKE IT CLEAR FROM THE VERY BEGINNING THAT I AM NOT

TESTIFYING FOR ANY PARTICULAR SET OF LEGISLATIVE PROPOSALS THAT HAVE BEEN ON THE TABLE. NEITHER AM I PREPARED TO ADVOCATE THAT THE GENERAL SORTS OF CHANGES I WOULD LIKE TO SEE BE MADE AT THIS PARTICULAR TIME. BOTH THE SPECIFIC CHARACTER AND THE DESIRABLE TIMING FOR STATUTORY REFORM ARE BEST JUDGED BY PEOPLE WHO HAVE CONTINUING CONTACT WITH THE ISSUES AND WITH THE LEGISLATIVE PROCESS. AS YOU WELL KNOW, I HAVE NOT HAD THAT KIND OF CONTACT. DESPITE THESE LIMITATIONS, HOWEVER, I THINK I MIGHT PLAY A USEFUL ROLE IN THESE PROCEEDINGS BY CITING SOME OF THE DEFICIENCIES IN THE FDA'S STATUTORY AUTHORITY THAT I ENCOUNTERED AS COMMISSIONER, AND BY DESCRIBING SOME OF THE RECOMMENDATIONS MY COLLEAGUES AND I DEVELOPED A FEW YEARS AGO TO IMPROVE MATTERS. THEY WERE PART OF A GENERAL EFFORT TO STRENTHEN FDA'S CAPACITY TO DEAL WITH FOOD SAFETY IN THE PUBLIC INTEREST.

BEFORE GETTING TO THE SPECIFICS, I WANT TO MAKE TWO MORE GENERAL POINTS ABOUT STATUTORY REFORM -- POINTS THAT I THINK ARE ESPECIALLY APPLICABLE TO CHAPTER FOUR OF THE FOOD, DRUG AND COSMETIC ACT. WE ARE TALKING ABOUT LEGISLATION WITH A LONG HISTORY, BOTH OF PERIODIC AMENDMENT AND OF ENERGETIC INTERPRETATION THROUGH REGULATION-WRITING. THE LAST SIGNIFICANT STATUTORY AMENDMENTS WERE MADE A QUARTER OF A CENTURY AGO, BUT THERE HAS BEEN NO DEARTH OF CREATIVE ADDITIONS TO THE CODE OF FEDERAL REGULATIONS. UNDER THESE CIRCUMSTANCES, THE LAW AND THE REGULATIONS OFTEN PASS BEYOND PUBLIC AND CONGRESSIONAL UNDERSTANDING, SO THAT EVEN SCIENTIFICALLY AND LEGALLY APPROPRIATE ACTIONS UNDER THE LAW PRODUCE A DEGREE OF PUBLIC CONSTERNATION THAT EMBARRASSES BOTH THE AGENCY AND THE CONGRESS. THAT IS EXACTLY WHAT HAPPENED IN THE CASES OF SACCHARIN AND NITRITE. THE VERY PROCESS OF STATUTORY REFORM, THROUGH EDUCATION AS WELL AS THROUGH LEGAL CLARIFICATION, SERVES TO RECALIBRATE OUR

UNDERSTANDINGS ABOUT THE LAW, ITS PURPOSES, AND HOW THESE PURPOSES MATCH THE PUBLIC'S EXPECTATIONS. AND IN THE COURSE OF STATUTORY REVISION, COMPLEX REGULATORY PROVISIONS CAN EITHER BE CODIFIED OR ELIMINATED. THE FOOD SAFETY LAWS AND THE REGULATIONS WRITTEN TO INTERPRET THEM ARE UNUSUALLY DIFFICULT TO COMPREHEND. THEY DEPEND UPON AN EXTREMELY COMPLEX TAXONOMY OF FOOD SUBSTANCES AND ADDITIVES, EACH TREATED IN A DIFFERENT FASHION UNDER THE LAW, AND OFTEN SUBJECT TO VARIOUS "GRANDFATHERING" PROVISIONS. AS NEW PROBLEMS HAVE ARISEN, THE AGENCY HAS ATTEMPTED TO SOLVE THEM SENSIBLY BY PROMULGATING REGULATIONS -- BUT THE BODY OF REGULATIONS HAS GRADUALLY BECOME A DENSE THICKET OF CONFUSION THAT BENEFITS NO ONE, WITH THE POSSIBLE EXCEPTION OF THE PRIVATE FOOD AND DRUG BAR IN YOUR CITY.

THAT DESCRIPTION, OF COURSE, COULD FIT THE DIFFICULTIES WE HAVE WITH MANY OLD LAWS. WHAT IS SPECIAL ABOUT THE FOOD, DRUG AND COSMETIC ACT IS THAT IT DEALS CENTRALLY WITH

MATTERS OF SCIENCE AND TECHNOLOGY. NOT ONLY ARE SCIENCE AND TECHNOLOGY NOT STATIC; THEY PROGRESS DIFFERENTIALLY, CREATING NEW PROBLEMS FOR OLD UNDERSTANDINGS. MUCH OF OUR PRESENT DIFFICULTIES WITH THE FOOD SAFETY LAWS COMES FROM EXACTLY THAT SORT OF DIFFERENTIAL SCIENTIFIC PROGRESS. ANALYTICAL CHEMISTRY HAS DEVELOPED MORE RAPIDLY THAN THE SCIENCE OF TOXICOLOGY, SO WE FIND OURSELVES IN A POSITION TO DETECT MORE THAN WE CAN EVALUATE, AND TO MEASURE MORE THAN WE CAN UNDERSTAND. AND THE SCIENCES OF EPIDEMIOLOGY AND OF QUANTITATIVE RISK ASSESSMENT, THOUGH STILL BARELY ADOLESCENT, ARE PREPARED TO CONTRIBUTE MUCH MORE TO THESE EVALUATIONS THAN THEY WERE WHEN THE FOOD SAFETY PROVISIONS OF THE LAW WERE LAST REVISED.

SO THE MATTERS WITH WHICH I THINK IT IS IMPORTANT TO DEAL AT SOME POINT IN A REVISION OF THE STATUTE ARE THESE:

- IS THE GENERAL SAFETY STANDARD OF THE LAW APPROPRIATE -- THAT IS, DOES IT SET A REASONABLE AND USEFUL THRESHHOLD FOR APPROVAL OF A FOOD ADDITIVE?
- DOES THE PRESENT LAW GIVE ADEQUATE SCOPE FOR SCIENTIFIC PROGRESS AND IMPROVEMENT OF TECHNIQUE? SHOULD THE AGENCY BE PERMITTED MORE DISCRETION IN THE TIMING OF ACTIONS IT PROPOSES?
- SHOULD THERE BE AN OPPORTUNITY TO CONSIDER BENEFITS IN DECISION-MAKING ABOUT FOOD SAFETY?
- SHOULD THERE BE SOME STATUTORY SPECIFICATION OF WAYS TO USE SCIENTISTS OUTSIDE THE AGENCY IN EVALUATING THE SCIENTIFIC BASIS FOR FDA'S DECISIONS?

LEVELS OF RISK

THE GENERAL STANDARDS OF SAFETY FOR FOOD ADDITIVES ARE

WISE, AND SURELY SHOULD BE RETAINED. THEY PUT UPON THE PROPONENTS OF USE THE BURDEN OF DEMONSTRATING THAT THE SUBSTANCE IS SAFE. TO THOSE BASIC PROVISIONS HAVE BEEN ADDED SOME MORE EXPLICIT ONES, THE BEST-KNOWN OF WHICH -- THE DELANEY CLAUSE -- EMBODIES A NUMBER OF SCIENTIFIC ASSUMPTIONS. IN PROHIBITING ANY AMOUNT OF A SUBSTANCE THAT HAS BEEN SHOWN TO "INDUCE CANCER IN MAN OR ANIMALS," FOR EXAMPLE, THE DELANEY CLAUSE STATES A VERY STRONG HYPOTHESIS ABOUT THE BIOLOGICAL SIGNIFICANCE OF VERY LOW DOSES.

MY OWN VIEW, WHICH I STATED ON A NUMBER OF OCCASIONS AT THE END OF MY TIME AS COMMISSIONER, IS THAT THE DELANEY CLAUSE IS UNDESIRABLY INFLEXIBLE IN TWO DIFFERENT WAYS. FIRST, IT LEAVES NO HEADROOM FOR SCIENTIFIC PROGRESS. SECOND, BY INCREASINGLY REQUIRING AGENCY ACTION UNDER CONDITIONS WHERE THE RISKS APPEAR TO BE TRIVIAL, IT INVITES PUBLIC RIDICULE AND DISREGARD FOR THE FOOD SAFETY LAWS MORE GENERALLY. I THOUGHT THEN THAT THE DELANEY AMENDMENT SHOULD

BE MADE MORE FLEXIBLE BEFORE IT BREAKS, AND I STILL HOLD THAT VIEW.

LET ME GIVE A SPECIFIC EXAMPLE OF THE SORT OF DIFFICULTY I HAVE IN MIND. IT SEEMS ALMOST CERTAIN TO ME, AS A BIOLOGIST, THAT SOME CARCINOGENIC SUBSTANCES WILL BE SHOWN TO BEHAVE AS THOUGH THERE WERE A BIOLOGICAL THRESHHOLD FOR THEIR ACTION. SUPPOSE A SUBSTANCE'S ROLE IS TO PROMOTE THE RELEASE OF A HORMONE, LIKE ESTROGEN, THAT ITSELF INCREASES THE LIKELIHOOD OF CANCER. IT WOULD NOT BE SURPRISING AT ALL TO FIND THAT SUCH A PROMOTING SUBSTANCE HAS NO EFFECT ON HORMONE RELEASE AT LOW LEVELS, BUT REQUIRES A CERTAIN CONCENTRATION IN ORDER TO TRIGGER THE CRITICAL EVENT. SIMILARLY, IT IS LIKELY TO EMERGE THAT CERTAIN SPECIES OF TEST ANIMALS ARE SIMPLY INAPPROPRIATE FOR DEMONSTRATING CARCINOGENICITY IN HUMANS OF CERTAIN CLASSES OF CHEMICALS, BECAUSE THEY LACK THE ENZYME SYSTEMS THAT, IN MAN, SERVE TO DETOXIFY THOSE COMPOUNDS. THE DELANEY CLAUSE

IN THE PRESENT LAW PROVIDES NO INCENTIVE WHATEVER TO SEEK OUT SUCH EXCEPTIONS AND JUSTIFY THEM SCIENTIFICALLY. ACCORDINGLY, I BELIEVE THAT THE LANGUAGE OF THE DELANEY CLAUSE SHOULD BE REVISED TO PERMIT MORE SCIENTIFIC DISCRETION IN DECIDING WHETHER A SUBSTANCE CAUSES CANCER. THIS COULD BE DONE BY CHANGING THE ABSOLUTE CHARACTER OF ITS PROHIBITION, SO AS TO PERMIT EXCEPTIONS IF THERE IS A SHOWING THAT THE CONCENTRATIONS TO BE FOUND OR EXPECTED CONTRIBUTE NO ADDED RISK.

"ACCEPTABLE" RISK

A MORE DIFFICULT QUESTION IS WHETHER THE GENERAL STANDARD OF SAFETY SHOULD BE CHANGED SO AS TO PERMIT RISKS THAT ARE INSIGNIFICANT, TRIVIAL, OR NEGLIGIBLE -- ALL TERMS THAT CAN BE FOUND IN RECENT LEGISLATIVE EFFORTS TO MODIFY THE FOOD SAFETY LAWS, AND ALL OF WHICH IMPLY THE ACCEPTABILITY OF SOME VERY SMALL AMOUNT OF RISK.

THIS IS A DIFFICULT QUESTION TO TALK ABOUT, PARTLY BECAUSE THE LANGUAGE IS ITSELF CONFUSING. THE CURRENT STANDARD IS "REASONABLE CERTAINTY OF NO HARM." YOU WILL NOTE THAT THIS IS ESSENTIALLY A PROBABILISTIC ASSERTION: IT CONCEDES THE POSSIBILITY OF ERROR IN OUR JUDGMENT ABOUT RISK, BUT STOPS SHORT OF SUGGESTING THAT A SMALL BUT CERTAIN RISK WOULD BE ACCEPTABLE. EFFORTS TO REINTERPRET OR REPHRASE THIS CONCEPT, IT SEEMS TO ME, OUGHT TO BE FORTHRIGHT. IT IS ONE THING TO SAY THAT WE CAN ACCEPT SOME SMALL PROBABILITY THAT OUR JUDGMENT IS INCORRECT, BUT QUITE ANOTHER TO SAY THAT WE ARE PREPARED TO ACCEPT CERTAIN RISKS AS LONG AS THEY ARE SMALL; THE SECOND FORMULATION RAISES, DIRECTLY AND IMMEDIATELY, THE QUESTION "HOW SMALL IS SMALL ENOUGH?"

I THINK IT IS ESSENTIAL FOR CONGRESS TO FACE UP TO THIS QUESTION. FOR TOO LONG, ALL OF OUR RISK STATUTES HAVE BEEN ALMOST DELIBERATELY VAGUE ON THIS POINT, SENDING AGENCY

HEADS OUT WITH INSTRUCTIONS THAT SOUND A LITTLE LIKE: "KEEP THE PEOPLE SAFE, BUT BE REASONABLE ABOUT IT." THAT SIMPLY REQUIRES THE AGENCY HEAD TO GUESS AT CONGRESSIONAL INTENT, AND THEN TO TAKE THE HEAT FOR THE CONGRESS IF THE GUESS TURNS OUT TO BE WRONG.

RISK ESTIMATION IS STILL A POORLY-UNDERSTOOD SCIENCE, AND IT ADDS TO ALL THE UNCERTAINTIES OF TOXICOLOGY THE ADDITIONAL DIFFICULTY OF TRANSLATING FROM ANIMAL EFFECTS TO HUMAN RISKS. NEVERTHELESS USEFUL -- THOUGH BROAD -- APPROXIMATIONS ARE POSSIBLE. I WOULD THINK THAT CONGRESS MIGHT WANT TO CONSIDER ESTABLISHING A DEFINITION FOR NEGLIGIBLE -- SAY, ONE ESTIMATED INCREMENTAL CANCER DEATH, LIFETIME, PER MILLION POPULATION. THIS RISK WOULD BE QUITE MODEST WITH RESPECT TO OTHERS THAT COULD BE PREVENTED BY VERY MODEST LEGISLATIVE INTERVENTION, E.G., BY LOWERING THE SPEED LIMIT BY A VERY SMALL AMOUNT. I AM NOT SO NAIVE AS TO BELIEVE THAT IT WILL BE EASY, OR EVEN LIKELY, FOR THE

CONGRESS TO LEGISLATE IN THIS WAY. I INTRODUCE IT HERE BECAUSE I THINK IT IS A LEGITIMATE PART OF THE DEBATE.

CONSIDERATION OF BENEFITS

I EXPECT THAT YOU WILL BE URGED BY SOME QUARTERS TO INCLUDE CONSIDERATION OF BENEFITS AS A PART OF THE REGULATORY PROCESS FOR FOOD ADDITIVES. THIS IS A MATTER THAT, IT SEEMS TO ME, OUGHT TO BE APPROACHED WITH A GREAT DEAL OF CAUTION. BOTH THE SACCHARIN AND NITRITE CASES SHOW THAT HEALTH BENEFITS CAN ENTER THE CONSIDERATION OF FOOD ADDITIVE SAFETY IN SIGNIFICANT WAYS. UNFORTUNATELY, "HEALTH BENEFITS" IS A DIFFICULT TERM TO DEFINE, AND IT CAN BE MADE EITHER SO NARROW AS TO BE USELESS OR SO BROAD AS TO BE LIMITLESS. MY OWN INCLINATION IS TO RECOMMEND THAT HEALTH BENEFITS BE CONSIDERED AND DEFINED FAIRLY BROADLY. BUT THAT HEALTH BENEFITS SHOULD BE CONSIDERED ONLY FOR THOSE ADDITIVES WITH A SUBSTANTIAL HISTORY OF USE IN THE FOOD

SUPPLY, AND WHERE THERE IS NO PRACTICAL SUBSTITUTE FOR THE ALREADY-USED ADDITIVE; AND THERE SHOULD BE A STRINGENT REQUIREMENT THAT THE HEALTH BENEFIT BE DEMONSTRATED, NOT JUST SHOWN TO BE PLAUSIBLE.

ARGUMENTS WILL NO DOUBT BE MADE FOR THE EXTENSION OF RISK/BENEFIT COMPARISONS TO INCLUDE ECONOMIC BENEFITS. I THINK THAT IS A VERY SLIPPERY SLOPE INDEED, AND I WOULD URGE YOU NOT TO WANDER FAR ONTO IT. RISK/BENEFIT BALANCING CAN ONLY BE CARRIED OUT SUCCESSFULLY IN A LIMITED UNIVERSE WHERE RISKS AND BENEFITS ARE MEASURED IN THE SAME KINDS OF UNITS. IT IS DIFFICULT TO COMPARE THE HEALTH BENEFITS ASSOCIATED WITH THE PROTECTION NITRITES PROVIDE AGAINST BOTULISM WITH THE HEALTH RISKS THEY IMPOSE. BUT AT LEAST WE ARE TALKING ABOUT THE SAME THING. CONSIDER HOW MUCH MORE DIFFICULT IT WOULD BE IF WE WERE ASKED TO WEIGH THE HEALTH RISKS OF A FOOD ADDITIVE AGAINST ITS DISTRIBUTED ECONOMIC BENEFITS! IF CONGRESS WERE TO GIVE SERIOUS CONSIDERATION TO

SUCH A PROVISION, IT SHOULD BE PREPARED TO STATE AT THE SAME TIME WHAT DOLLAR VALUE IT PLACES UPON A SINGLE HUMAN LIFE. WITHOUT THAT, CONGRESS WILL BE MAKING AGENCIES ACCOUNTABLE FOR A PROCESS CONGRESS IS ITSELF UNWILLING TO DEFINE.

TIMING OF ACTIONS

WE DID LEARN FROM THE NITRITE EPISODE THAT FDA LACKS ADEQUATE DISCRETIONARY AUTHORITY WITH RESPECT TO THE TIMING OF BANS. YOU MAY RECALL, MR. CHAIRMAN, THAT IN VIEW OF THE IMPORTANCE OF NITRITES IN PROVIDING PROTECTION AGAINST BOTULISM AND THE NEED FOR TECHNOLOGICAL TRANSITION IN THE INDUSTRY, WE PROPOSED TO PHASE OUT THE USE OF THOSE FOOD ADDITIVES OVER A PERIOD OF THREE YEARS INSTEAD OF IMMEDIATELY. THE JUSTICE DEPARTMENT, UNFORTUNATELY, TOLD US THAT IT HAD NEVER HEARD OF A DANCE CALLED THE SLOW DELANEY; AND A REASONABLE APPROACH TO A TROUBLESOME PROBLEM WAS RULED OUT. I WOULD HOPE THAT CONGRESS WOULD CONSIDER GIVING THE

AGENCY AUTHORITY FOR A PHASE-OUT, PERHAPS LIMITED TO A FEW YEARS AND TO THOSE ALREADY EXISTING ADDITIVES FOR WHICH THERE IS NOT A REASONABLY PRACTICABLE SUBSTITUTE.

PEER REVIEW

THE DECISIONS MADE BY A SCIENTIFIC REGULATORY AGENCY NEARLY ALWAYS REST ON JUDGMENTS OF PROBABILITY AND NOT CERTAINTY; IT IS SOMETIMES NECESSARY TO DECIDE, EVEN WHEN THE DATA ARE NOT AS COMPLETE OR CONVINCING AS YOU WOULD LIKE. SINCE SOME PARTIES ARE INEVITABLY GOING TO DISLIKE ANY DECISION, THERE IS ALWAYS ROOM FOR REINTERPRETATION AND RECALCULATION. UNDERSTANDABLY, SOME OF THOSE NEGATIVELY AFFECTED BELIEVE THAT A SYSTEM FOR EXTERNAL PEER REVIEW WOULD OFFER AN ADDED GUARANTEE AGAINST UNWISE OR UNFAVORABLE REGULATORY JUDGMENTS.

PERHAPS IT WILL -- BUT NOT WITHOUT SIGNIFICANT COST. IT EXTENDS THE OPPORTUNITY FOR SECOND-GUESSING, AND MAY

PROLONG NEEDED ACTIONS. IT MAY ALSO REDUCE THE INCENTIVE FOR GOOD SCIENTISTS TO DO THEIR WORK INSIDE THE AGENCY, BY IMPLYING THAT THEIR JUDGMENTS ARE OF INTRINSICALLY LOWER WORTH THAN THOSE OF OUTSIDERS. I THEREFORE REGARD THIS PROPOSAL AS A MIXED BLESSING, AND URGE THAT IT BE GIVEN A CAUTIOUS AND SKEPTICAL READING.

IF THERE IS TO BE A FORMAL ORGANIZATION FOR PEER REVIEW, I THINK THE BEST PLACE TO PUT IT IS CLOSE TO THE AGENCY, IN THE FORM OF AN ADVISORY COMMITTEE SIMILAR TO THOSE EMPLOYED BY FDA'S BUREAU OF DRUGS. THE AGENCY SHOULD RETAIN THE OPTION NOT TO REFER TO SUCH A COMMITTEE ANY MATTER THAT IT CONSIDERS RELATIVELY UNIMPORTANT. A CLOSE RELATIONSHIP BETWEEN THE AGENCY AND THE ADVISORY COMMITTEE WOULD ENSURE THAT MATTERS GET REFERRED RELATIVELY EARLY IN THEIR CONSIDERATION. IT WOULD ALSO PROVIDE ANOTHER IMPORTANT GUARANTEE: THAT THE MEMBERS OF THE REVIEW GROUP WOULD BE CHOSEN WITH FDA PARTICIPATION, AND WOULD BE SUBJECT

TO CONFLICT-OF-INTEREST AND OTHER PROVISIONS THAT APPLY TO GOVERNMENT ADVISORY COMMITTEES GENERALLY.

FINALLY, I WOULD URGE YOUR ATTENTION GENERALLY TO THE PARTS OF CHAPTER 4 THAT DEAL WITH FDA'S AUTHORITY TO ACT. AS WE MAKE THE STANDARDS FOR SAFETY MORE FLEXIBLE AND BETTER ATTUNED TO MODERN SCIENCE, WE SHOULD AT THE SAME TIME IMPROVE THE CAPACITY OF THE AGENCY TO REMOVE UNSAFE PRODUCTS FROM THE MARKET EXPEDITIOUSLY, TO CONDUCT INSPECTIONS, AND TO TRACE HAZARDS MORE EFFECTIVELY.

MR. CHAIRMAN, I HOPE THESE THOUGHTS ARE USEFUL TO YOU. I AM GRATEFUL TO YOU AND YOUR COLLEAGUES FOR HOLDING THOROUGH HEARINGS ON THIS VERY IMPORTANT SUBJECT. THERE IS NOT A TRICKIER OR MORE CONTROVERSIAL AREA IN WHICH TO LEGISLATE THAN THE AVOIDANCE OF PUBLIC HEALTH RISKS; AND THE FOOD SAFETY LAWS ARE, IN A WAY, OUR MODEL FOR DEALING WITH THAT AREA. AFTER FOUR YEARS AWAY FROM MY OWN RESPONSIBILITIES IN THIS AREA, I AM STILL CONVINCED THAT IT

IS ABOUT AS IMPORTANT A JOB AS ANYONE CAN UNDERTAKE. YOU ARE DEALING WITH A STATUTE THAT IS BASICALLY SOUND; IT NEEDS ONLY SOME TUNING TO MAKE IT CONFORM TO CONTEMPORARY SCIENTIFIC REALITY. THE AGENCY RESPONSIBLE FOR ADMINISTERING THAT STATUTE IS ALSO SOUND, AND FULL OF ABLE AND DEDICATED PEOPLE. THEY DESERVE THE VERY BEST TOOLS YOU CAN GIVE THEM TO WORK WITH.

THANK YOU VERY MUCH.

The CHAIRMAN. Thank you, Dr. Kennedy.

Dr. Goyan, we will turn to you at this time and take your testimony, and then we will have some questions for both of you.

STATEMENT OF JERE E. GOYAN, PH. D., DEAN, SCHOOL OF PHARMACY, UNIVERSITY OF CALIFORNIA, AND FORMER COMMISSIONER, FOOD AND DRUG ADMINISTRATION

Mr. GOYAN. Thank you very much, Mr. Chairman.

I, too, am grateful for the opportunity to appear before this distinguished group and take part in what I suspect will become the great debate over the food safety portion of the Food, Drug and Cosmetic Act.

When I left Washington, it was reported in the Washington Post that I had shown very little interest in food matters. I found that somewhat amazing in view of the fact that, in the short time I was Commissioner, I did rule on FD&C Red No. 2, on cyclamate; I took part in debates on aspartame, on nitrites; I had to deal with caffeine as a potential teratogen; with the packaging material Bric Pac and the use of lead acetate.

Thus, I feel I have had considerable experience in the area, and found it to be an absolutely intriguing—not to say difficult—area.

Rather than go over my formal comments, I thought I would just speak to a few of what I consider to be the truly important issues that this committee is going to have to face.

The CHAIRMAN. In that regard, we will put your formal comments in the record as though fully delivered. We appreciate that.

Mr. GOYAN. Thank you.

Probably the most important issue, is the definition of what we mean by safe. Certainly it is not quantifiable in any way, and thus we have to turn to the obverse and talk about risk in some fashion.

The general safety clause, as Dr. Kennedy pointed out, says that the agency must make certain that foods are such that there is a reasonable certainty of no harm. Judge Levinthal, in his decision relative to acrylonitrile, referred to a, quote, de minimis risk, and I understand one of the most current proposals says, and I quote, a reasonable certainty of insignificant risk.

Now, I would maintain that all of these, to some degree, beg the question. For example, what is the difference between no harm and insignificant risk? Or what is a reasonable certainty? Perhaps we could turn to Lewis Carroll and say a reasonable certainty is what the Commissioner says is a reasonable certainty, but I recall that someone in the agency at one point pointed out that if you look at the general safety clause, your approach to it depends a lot on whether you emphasize the term reasonable, the term certainty, or the term harm.

Thus, we are faced with a very difficult question: How do we approach it? Well, with noncarcinogens, there is rather general agreement. What we do is we determine what the toxicity of the substance might be, we then determine what we refer to as the no-observable-effect level, usually referred to as NOEL, and then we divide that by 100 and say that that will be the acceptable daily intake of this particular foodstuff. And, surprisingly, very few people ever debate about that. But when we come to substances which cause cancer, carcinogens, the debate intensifies considerably.

Why is that true? The agency has maintained over the years that the general safety standard, that is a reasonable certainty of no harm, was such that certainly they could never approve a carcinogen. No one would argue that getting cancer is not harmful. However, during the debates on food additives and food safety in 1958, Congressman Delaney insisted on putting into the law his now famous Delaney clause, which is basically a no-risk clause. It says, as you all know, that if a substance causes cancer in man or animals, it must be banned from the food supply. It does give one small out for the Commissioner, for the agency, in that it says that if after a fair evaluation of the data, the Commissioner reaches the conclusion that it causes cancer, then he has no options.

You need to understand that this creates a certain milieu within the agency, regarding carcinogens. Perhaps I can illustrate it with an experience from my own time in office, relative to a food packaging method called Bric Pac. Bric Pac is that cardboard box that you now see in grocery stores that carries liquids. It is done by using a plastic material inside the cardboard that is sealed, and thus you can maintain the fruit juice or other liquids for long periods of time.

The problem the agency had in approving Bric Pac is that the plastic material had to be sterilized prior to use—it couldn't be done by heat or anything of that nature— so the company that was producing it was doing it with the use of hydrogen peroxide.

Now, hydrogen peroxide, certainly diffused into the plastic during the time that it was in contact with it, and then when the plastic comes in contact with the foodstuff, it will diffuse back out. Thus, it becomes what the agency refers to as an indirect food additive, and although the agency was perfectly well aware that it would be a very small amount of hydrogen peroxide—the proponents actually argued that there would be none—but it would be there. They nonetheless would not approve it for a long period of time as the debate went on: Is hydrogen peroxide a carcinogen and therefore under Delaney and therefore unapprovable?

In discussions after I became Commissioner, I became aware of the fact that there was no one in the Bureau of Foods that believed it was a safety hazard; that is, everyone was convinced that in spite of the one study that appeared, at very high doses, to cause cancer from hydrogen peroxide, that this was not indeed a true safety hazard.

In other words, a fair evaluation of the data did not find it to be a safety hazard, and therefore we were able to approve the material, but it was after what I would consider almost unconscionable delays.

The other problem that we have had with Delaney that all of you have spoken to previously, is the fact that our analytical techniques are getting better and better. They are getting to the point where they are almost frightening in terms of the fact that someday we will probably be in the position where we can pick up a few molecules in a gram, and that means that basically we might end up having to ban the entire food supply, obviously not something that any of us believe should happen.

There are also differences in the science today over what it was in 1958 in the sense that we know there are differences in carcinogens. They don't all act by the same mechanisms, and indeed in the case of promoters there is a good probability that there may be a threshold; an idea that none of us has been willing to countenance in terms of initiators of cancer.

Therefore, I think this committee needs to return to the basis of our original desire, and that is for reasoned and reasonable protection of the public. This is truly a great public policy decision which should be made by the Congress of the United States. I think that what we need to look at is what do we mean by insignificant risk or what I have on occasion called toxicologic zero, rather than analytical zero, or what Judge Levinthal referred to as a de minimis risk.

We are fortunate in that our science has advanced to the point where we can do risk assessments with regard to carcinogens and arrive at what is sometimes referred to as the worst plausible estimate of the carcinogenic risk, I would rather say it's the best plausible estimate of its safety—and from that we use some sort of decisionmaking limit such as the one in a million increased risk over a lifetime, as Dr. Kennedy proposed as a possibility.

It is important, however, that everyone understand that when we say that there is 1 chance in a million, it is really much less than 1 chance in a million, because we always use the most conservative methods of estimation, and indeed I could not personally maintain that there is any real difference between 1 in a million, 1 in ten million, and one in a hundred million. When you get to that point, it is very unsure.

Essentially, then, you have arrived at what I would call toxicological zero or a point of insignificant risk, and it's something that I hope the Congress will address directly.

This is a much stricter standard than we use for the acceptable daily intake, the ADI for other types of possible toxicities, and I think it is appropriately so, for all of us, believe that cancer is one disease from which we want to do everything possible to protect the public.

Let me take one more example from my own experiences, and speak to the issue of lead acetate, better known, probably, to the people in the room as Grecian Formula. I hasten to add, as you can see I do not use it. [Laughter.]

This particular substance had been before the agency for a number of years when I arrived. It is an external color additive which brings it under a Delaney clause that is slightly different than the other Delaney clauses. In discussing the issue, again with the people in the Bureau of Foods, there was unanimity in the belief that there was no problem with the use of this particular substance; indeed, risk assessment showed that the greatest the increased risk could be was something like 1 in 5 million over a lifetime, and therefore, we went ahead and proposed to approve it.

The Delany clause is one of the most important and most difficult decisions the Congress will be facing this year, and I hope that you all will face it directly.

There is another thing that the agency has to deal with, and that is priority setting. In my experience at the agency, too often we found ourselves spending immense amounts of time on what were essentially trivial public health problems, while at the same time, not being able to spend as much time as we should have on real problems. One of the ways that was proposed by Dr. Kennedy and his group at FDA, was that foods be divided into three regulatory groups rather than the present nine, where you would have traditional foods, which would come under the ordinarily injurious clause, the food contaminants which would use tolerances, and food additives which could be regulated as presently under section 409 or with some sort of new definition of toxicologic zero.

Now, with regard to benefits, I would simply like to say that I am personally only willing to talk about benefits that are health benefits and which accrue to the same person who takes the risks; that is, in the case of nitrites, for example, if I take the risk of cancer because I don't want to take the risk of botulism, that is a perfectly reasonable thing to do, but I don't want to have the benefit accrue to someone else, rather than to me, if I take the risk.

With regard to the issue of peer review, I would certainly agree with what Dr. Kennedy has said: Every Commissioner wants and needs the best science possible, in order that he can make a wise decision. Indeed, when we were dealing with the problem of caffeine, we did call for an outside peer review before we moved forward. However, I would again caution not just the Congress but those who so enthusiastically press for peer review that it may not be the panacea they believe. As a scientist myself I know that we are raised in a milieu which essentially says that nothing is ever totally proved. Thus, if I set up a peer review group, I will almost guarantee it will always find whatever you bring before it as not proved. Thus, whoever is carrying the burden is going to be the one that has the hard time—that is, if I am from industry, I have a food additive that is under question, I would like to have peer review, because I am sure a peer review group would say that the agency has not proven that it is a problem.

On the other hand, if I was with industry and was trying to get a new substance approved, I wouldn't want to have peer review because the scientific peer review group will say, gee, this hasn't been proved to be safe. So, I would caution as Dr. Kennedy has, very careful thought about this, and also add that if you are going to require peer review for everything that comes up, it will slow down the process.

I believe, having read the testimony of a number of people that are going to be appearing before you, that we are reaching slowly a consensus in this particular area, and I hope that you can move forward expeditiously and make some changes in the law.

Thank you very much.

[The prepared statement of Dr. Goyan follows:]

TESTIMONY OF JERE E. GOYAN, PH.D.

DEAN, SCHOOL OF PHARMACY, UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
FORMER COMMISSIONER, FOOD AND DRUG ADMINISTRATION

PRESENTED BEFORE THE U.S. SENATE COMMITTEE ON LABOR AND HUMAN RESOURCES

June 8, 1983

MR. CHAIRMAN AND MEMBERS OF THE COMMITTEE:

There have been a number of reports, symposia and hearings on the subject of food safety over the past several years, most if not all of which, I assume, have been made available to the Committee. I will not, therefore, attempt a dissertation on this topic, but rather will address a number of food safety issues as seen from my perspective as a former Commissioner, and will attempt to identify those which I believe need public discussion and perhaps changes in legislation.

There is no doubt in my mind that everyone, whether he be consumer, regulator, food manufacturer or processor, wishes to maintain a safe food supply. There is less unanimity, however, on what "safe" means. And for very good reasons. Attorneys, for example, may define "safe" as "a reasonable certainty of no harm," and then turn to science for the development of the precise implementing criteria. Yet scientists trained in quantitative measurement find it difficult to extrapolate such concepts with the precision required.

Recent suggestions of a different definition such as "a reasonable certainty of insignificant risk," may sound less stringent, but--depending on regulatory implementation--could in fact be equally as strict. The problem is that although we have ways of quantitating risk (albeit in only an approximate manner), there is no way to quantitate the concept of safety. Thus one is led inevitably to defining safety in terms of lack of risk at some arbitrary level. As an example, over the last several years, the FDA has attempted to define as safe an animal feed additive whose risk for increasing the incidence of cancer in the ultimate consumer of the animal is "less than one chance in a million over a lifetime." There seems to be among most people an inherent feeling that such a level of increased risk is reasonable, whereas an increased risk of one in 100,000 might not be. It seems to me an intelligent approach.

Given an agreeable definition of safety such as that previously mentioned for all possible toxicological hazards, including mutagenicity, carcinogenicity, teratogenicity and other such undesirable manifestations, one superficially appealing approach would be to test all of the substances presently ingested as foodstuffs and to permit on the market only those substances that meet the criteria. Indeed, this was basically the approach suggested by the National Academy of Sciences in it's report in response to the Saccharin Study and Labeling Act. As logical as this may seem to some, the recommendation suffers from two flaws. First, we lack the scientific knowledge to make all of the judgments required, and, second, the amount of time and scientific resources needed would be massive. The difficulty with most of the problems related to food toxicology is that we are dealing with what might be described as intermediate science, that is to say, a phase that every science passes through, where much is known, but much remains to be known. Take, for example, the problem of determining the potential mutagenicity of a given substance. A mutagen is an agent that adversely affects chromosomes, the transmitters of heredity. Although we have methods for determining mutagenicity, they are fraught with error. The same tests carried out by different laboratories often provide different results and different methods likewise may result in opposing findings. Furthermore, as of now, no one really knows the actual significance of a finding that a given substance is mutagenic in a test system. We are left with such disturbing unanswered questions as: Is the problem reversible and therefore of little or no toxicological importance, or does it result in a change in the genetic code of an individual, and therefore ricochet down the generations? We frankly don't know because we are talking about intermediate science.

What, then, can be done until a more adequate scientific data base is developed? It is obvious, as indeed commentators of all persuasions on this issue have noted, that some priorities must be set. One should start by focusing the effort on identifying the food substances most likely to be hazardous. It seems to me a poor allocation of effort at this time to dilute our resources by concerning ourselves with those substances of long standing that are unlikely to be of toxicological significance. These can be meticulously scrutinized at a later time. Along this line, in the past FDA has considered the establishment of three mutually exclusive categories of food substances. These proposed categories reflect the basic distinctions among food substances that justify a different regulatory approach for each. The categories are traditional foods, food contaminants, and food additives. Such a categorization greatly simplifies the present system consisting of nine different legal categories of food substances, and would prioritize FDA's efforts in a manner that would maximize public safety and the availability of a nutritious food supply. For example, FDA would have to prove that a traditional food was ordinarily injurious before it could be banned. On the other hand, food contaminants would continue to be regulated by the establishment of appropriate tolerances for such unavoidable substances, whereas food additives (substances that are added to the food supply during manufacture, processing or packaging) would continue to be regulated as presently done under Section 409 of the Food, Drug and Cosmetic Act.

Contained within Section 409 is that most difficult and perplexing subsection known as the Delaney Clause, which provides that no food additive shall be approved "if it is found to induce cancer when ingested by man or animal." Although few other sections of the Food, Drug and Cosmetic Act have been lavished with such notoriety, in point of fact, the Delaney Clause is simply an operational statement aimed at achieving what every American has the right to expect: that the foods he or she ingests will not increase their risk of cancer.

There is no question that the Delaney Amendment was appropriate when it was enacted in 1958, a time when it was generally believed that there were only a few carcinogenic food substances, and when analytical techniques were relatively limited and when all cancer causing substances were assumed to act by an identical mechanism. Today, however, we know that many chemicals are capable of increasing by differing mechanisms the rate of cancer in animals--although not necessarily in humans--and analytic technology has advanced to the capability of measuring such substances in parts per trillion. As a hypothetical example of what is possible today, let us assume that we determine that an important food additive at its present level of use is capable of increasing the rate of cancer by one in one thousand million over a lifetime. Strict interpretation of the Delaney Clause would dictate that the substance be banned from the food supply. Now I, for one, would not agree with such an action, and it is because of this--the fact that Delaney is not sensitive to advances in technology--that I believe that it has lost much of its initial utility.

It seems to me to be time to return to the real issue that the Delaney Clause sought to address: reasoned and reasonable protection of the public. In order to do so, it may be necessary for Congress to authorize FDA to establish levels of "toxicological zero" for food substances. The value of "toxicological zero" might range between absolute zero (as currently dictated by the Delaney Clause) to some value such as the guideline discussed above, namely one chance of an adverse outcome in a million over a lifetime.

A public policy decision as to the level which would constitute "toxicological zero" for carcinogens should be made by the people of the United States speaking through their elected representatives for it must be a subjective decision. Such a definition would, I think, allow FDA to provide maximum protection for the American Public, while guaranteeing a plentiful food supply.

A subgroup of additives that have caused regulatory activity all out of proportion to their potential impact on health are the so called "indirect food additives." These are substances which tag along as trace ingredients of major additives, or which migrate from packaging material and because of their small amounts are generally of little toxicological consequence. An example of this is the difficulty that arose over the use of acrylonitrile copolymer bottles. From a packaging and conservation point of view, these were highly attractive alternatives to glass bottles. They were lightweight, shatterproof, and could be recycled. Unfortunately, acrylonitrile monomer is highly toxic, and although no molecules of this chemical could be detected in the solutions packaged in it, an irrevocable scientific principle known as Fick's Law guaranteed that some of this substance would eventually migrate into the foodstuff. As a result, the Agency banned the acrylonitrile polymer bottle. That decision was challenged in the courts which in turn referred it back to FDA on the grounds that it might be a de minimus (or negligible) risk and asked the Agency to address the question of whether or not it was de minimus.

Since the original action in 1977, acrylonitrile monomer has been shown to be a carcinogen and thus would now come under the Delaney Clause. Absent a change in the Clause to establish a new "toxicological zero", it appears that the Agency will not be able to allow the use of this material despite its attractiveness and the earlier court decision.

Earlier, I alluded to the report of the National Academy of Sciences. In it is a recommendation that a proposed food additive also be assessed for its potential benefits before being banned. Among the suggested potential benefits to be assessed were "physiological, psychological, or economic." Although there is no doubt that all such benefits are possible, I cannot accept the recommendation that economic benefits to a producer should be a consideration in the banning process. It was my firm belief as Commissioner (and continues to be my belief) that it is the consumer who takes the risk when ingesting an additive, and his or her health should be the only consideration. It matters little to the consumer injured by a food additive whether the offending ingredient saved the producer some money.

Only direct health benefits which accrue to the same individual who takes the risk by ingesting the additive should be considered in any decision relative to banning the additive. The best example of this is the risk from using nitrites as a preservative (nitrites can form small amounts of nitrosamine, a known carcinogen) balanced by the preservative effect of nitrites in preventing botulism (especially since no alternative preservative is known). A balancing of such risks and benefits is not possible under present law, but would be a welcome addition to the FD&C Act for additives presently in use whenever new questions arise concerning their potential toxicity.

It is important for Congress to consider carefully the effect of changes in the law upon the credibility of the Agency. For example, if Congress were to mandate some form of risk benefit analysis without carefully delineating what sort of benefits should be acceptable, the Agency would be placed in a "no-win" situation. No matter what decision the Agency might make, relative to a proposed benefit, some part of its constituency would be very unhappy, for such determinations require broad value judgments which are more properly made by an elected body.

When one considers the "flap" which occurred when FDA properly proposed to ban saccharin as required by Delaney one can hardly imagine the outcry when FDA might suggest they planned on allowing the continued use of a carcinogen because of its importance in maintaining the shelf stability of a product!

The process of banning a foodstuff is always a complex one, heavily dependent upon the category of food being considered. However, at some point it always comes down to a recommendation from the Bureau of Foods to the Commissioner for final action. The nature of science and regulatory activity is such that banning decisions must always be made before the science is complete (if it ever is) and is thus bound to be controversial, especially if it affects an economically important segment of the food supply. The experience of the past few years, especially with saccharin and nitrites, has led some to believe that such problems would go away if FDA were required to have some form of outside peer review. It is true, of course, that the Agency in general and the Commissioner in particular wants the best science advice possible, and on occasion requires outside verification and support for a proposed decision. However, I fail to see how an automatic peer review system can do much, other than to delay the process in the vast majority of cases, with no net gain. Those of us who come from the milieu of academic science (the body from which such peer review would be sought) have an ingrained bias that does not match the needs of a regulatory agency. We are all trained in the scientific method, a persuasion that instills the firm belief that nothing is ever conclusively proved, and more studies would make a decision clearer. Tactically speaking, if I were a producer seeking the approval of a substance, I would never want an outside peer review since it would probably find my case for the safety of the substance "unproved." If, on the other hand, one of my previously approved and economically important substances were under fire by FDA, I would most assuredly endorse outside peer review which would again probably find the case "unproved". For these reasons, I cannot endorse the suggestion that outside peer review be required.

It is important that everyone understand that the rulemaking process is currently designed to allow those who disagree with a proposed action to present their case. During the "notice and comment" phase of rulemaking, every interested party has the opportunity to provide argument in support of or opposed to a particular action. Any substantive argument, especially that which is backed by hard data, must be addressed by the Agency before making a final decision. Furthermore, even prior to such rule making, it is generally well known throughout the industry that action is being contemplated. (This comes about because any decision must be based upon scientific evidence of potential toxicity, as such evidence appears in the scientific literature the sponsor is alerted. In some cases FDA will alert the appropriate sponsors by raising questions as to new findings with them.) Thus, it is possible for a sponsor to approach the Bureau prior to rule making if they wish to present facts which they believe are germane to the decision. This fair and open system is an additional reason why I do not believe that some form of required outside peer review prior to decision making is necessary. It would only complicate the process and do, perhaps, more harm than good.

The food safety law is certainly one of the more complex sections of the FD&C Act. Indeed, some Have maintained that is is understood by only a half dozen people in the United States! Be that as it may, the record shows that the FDA has done a remarkably good job of balancing the various factors involved and maintaining the safety of the food supply. I am not at all sure that the legal thickets need clearing with a totally new law. It would seem to me that the Congress would be better advised to fine tune the existing law by proposing a series of amendments that focus in on the core issues that I raised today. Such an approach would assure careful examination of each of the proposals and, hopefully, avoid the potential problem of a new law causing more problems than it solves.

The CHAIRMAN. Thank you so much, Dr. Goyan.

Let me ask you both this question. Should the changes in food policy advocated in your testimonies be made administratively by the FDA or legislatively by the Congress?

Dr. KENNEDY. Well, Jere is giving me first shot at it.

Not everybody, Mr. Chairman, agrees with the philosophy I am about to present to you. I think that there is often an argument made for a lot of agency discretion, and preference is often expressed for administrative rather than legislative procedures when those are possible.

The risk one runs, if that goes on too long, is the one I cited; namely that the law and the body of regulations that are built on it simply get out from under the capacity of any person to scrutinize it, to hold it in the mind, and to understand where the agency has really gone.

I think some of the most difficult circumstances that I faced as commissioner were not so much in looking at new scientific findings on a troubled substance, though those drew most of the fire and attention. I think that they were circumstances in which I discovered that a body of regulation had grown up that was so complicated and arcane that half the people in the agency did not understand it; I did not understand it; the Members of Congress that were on my oversight committees did not understand it; and certainly the public and the regulated industry did not understand it.

Once regulations built on a simple statute get that complicated, the agency is running real risks of being misunderstood by its own overseers. That is the worst position for an administrator of a Federal agency to be in.

So my view of the matter is that the really critical distinctions—the risk standard, the definitions of what kinds of risks are acceptable, matters of that sort—really have to be enunciated by the Congress. That is what the people elect you for. They don't vote for the Commissioner of the FDA or the Secretary of Health and Human Services. They do expect you to reflect their values with respect to the risk averseness of the society.

And so I think it is very important that with regard to those essential underpinnings, the Congress express itself clearly.

The **CHAIRMAN**. Thank you. Would you respond to that, Dr. Goyan?

Mr. **GOYAN**. I agree entirely with Dr. Kennedy in this regard.

I think that the commissioner finds himself getting dangerously close to legislating by continuous regulatory changes.

The **CHAIRMAN**. Well, thank you.

Some have argued that the FDA, because of the strings that exist between the current statute and the technological advances, has on a number of occasions resorted to "creative interpretations" of the law to reach sensible results.

Now, would either of you care to comment on that viewpoint?

Mr. **GOYAN**. I would only say that that is absolutely true.

Dr. **KENNEDY**. I, too, Mr. Chairman, confess to occasionally yielding to creativity. [Laughter.]

You cannot exist out there without it. And if you don't do it, you may be certain that your chief counsel will. [Laughter.]

Mr. **GOYAN**. Actually, Mr. Chairman, I was speaking for Dr. Kennedy. He did it; I never did. [Laughter.]

The **CHAIRMAN**. What changes in the statute would, in your opinion, improve the credibility of the agency decisionmaking with consumers, scientists, and the food industry? Now, you have basically covered that, but if we could be even more specific, I would appreciate it.

Dr. **KENNEDY**. Well, I think what it really requires is a certain amount of priority description. I tried to arrange my testimony in what I considered the priority order.

The various risk standards—and particularly any quantitative evaluation that the Congress can attach to them—I think that is the core issue. It is more important than any other single matter.

The **CHAIRMAN**. Do you agree, Dr. Goyan?

Mr. **GOYAN**. I would say that I again agree with Don. Probably the most important issue that you are going to have to face, and the most difficult politically, is the question of the Delaney clause.

The **CHAIRMAN**. It has been said that the present statute is too rigid. I would like to have your comments on your experiences and observations during your tenures as Commissioners with regard to whether or not the statute is indeed too rigid.

Now, both of you have alluded to this question in your statements. Why don't we start with you first, Dr. Goyan?

Mr. **GOYAN**. Well, I think that I did speak to that rather directly in my comments with regard to substances like lead acetate. It is indeed rigid and difficult to deal with. I am not sure, however, that it is rigid to the point that it cannot be worked with. Certainly we were able to do something in that particular case.

But the question of the risk, of definition of risk or definition of safety, if we look at the other side, is one that we do need. I don't think, the term is flexibility. We need guidance.

The CHAIRMAN. All right.

Dr. KENNEDY. Maybe it would be helpful if I mentioned a problem we have that I don't think would be fixed by simply making the Delaney clause more flexible in the ways I have suggested. I say it so that I can make one last lunge at a problem that continuously evaded me during my time here.

That was getting people to understand that, although the agency proposed to proceed in regulating saccharin—before Congress enacted the moratorium—on the basis of the Delaney clause, the Delaney clause was sufficient but not necessary with respect to that action. That is, the general food safety standard would have been more than adequate to trigger an agency procedure to remove saccharin from the "generally recognized as safe" list, in the first instance, and then to ban it or restrict its use in the ways that FDA actually proposed.

So the Delaney clause, although it is frequently cited as the most irrational and inflexible part of the food safety laws by those who are particularly distressed about it, has actually not been invoked very frequently. It would be unfortunate if people got the idea that merely by making the Delaney clause more flexible, one will emerge with a set of food safety laws that are very much more lenient. The general risk standard that exists under present law is a tough standard and would have, by itself, been adequate in the saccharin case.

Mr. GOYAN. I wonder if I might just add one point.

The CHAIRMAN. Certainly.

Mr. GOYAN. It is important that you understand that the one-in-a-million-over-a-lifetime standard is such that saccharin could not be approved under that standard.

The CHAIRMAN. In an editorial in the Wall Street Journal entitled "Beer Causes Cancer," it was stated that:

> Unless public health types start making some more reasonable distinctions between tolerable and intolerable cancer risks, an awful lot of people are going to decide that they would just as soon stop worrying about the whole subject and have another beer.

Now, isn't there some truth, really, to their concerns here?

Mr. GOYAN. Perhaps I should speak to that since that occurred while I was Commissioner.

The CHAIRMAN. Go right ahead, Mr. Goyan.

Mr. GOYAN. I would point out that we did not ban beer. [Laughter.]

We did achieve a much more desirable situation in that beer no longer contains nitrosamines in any measurable amounts because the industry was able to find other ways of getting it out of the beer.

I am rather proud of what the Bureau of Foods was able to obtain in that particular case and what the industry did.

The CHAIRMAN. Well, thank you.

Dr. Kennedy, in your testimony, you say, "We find ourselves in a position to detect more than we can evaluate and to measure more than we can understand."

Now, could you elaborate on that, and discuss how we can handle this problem?

Dr. KENNEDY. Before I do that, do I get to go back one question and take my swat at the Wall Street Journal?

The CHAIRMAN. Sure.

Dr. KENNEDY. I mean, I would really leave this hearing feeling frustrated if I didn't get a chance to point out that——

The CHAIRMAN. That is fine. It may not be fine with the Wall Street Journal, but it is fine with me. [Laughter.]

Dr. KENNEDY. The wording in that editorial expresses exactly the confusion that I am trying to point to. It says, "If public health officials will only be more reasonable in their definition of risk."

Public health officials, at least the ones who work in the agency that we are talking about here, are accountable to the Congress of the United States, which is the expressor of the public's wish about how risk-averse it is. It is the Congress that has to make that decision, responding to the electorate with respect to the level of safety, and then the public health officials can exercise their responsibility to estimate the risks and then to proceed against them to remove them from the environment.

I think the Journal somehow believes that the Commissioner of the FDA governs in this respect. What I am advocating to you is that the Commissioner of the FDA ought to be carrying out the people's wishes, transmitted through congressional oversight and legislation on the matter of how much risk we find acceptable.

The CHAIRMAN. What about that second question?

Dr. KENNEDY. Oh, yes.

The CHAIRMAN. Basically, it was that we find ourselves, as you stated in a position to detect more than we can evaluate and to measure more than we can understand. Now, could you elaborate a little bit on that and discuss how we can handle this situation.

Dr. KENNEDY. Well, again, I think that the central part of the solution is providing at least a band of congressionally determined acceptable risk so that we could then begin to decide, for example, how much of the migration of a prospectively carcinogenic or teratogenic monomer from a plastic packaging material could be permitted under expected conditions of use.

I think that establishing that kind of flexibility would be highly desirable and that it would remove us from that particular dilemma. It is, as Jere said, knowing what could be considered de minimis in Judge Levinthal's terms, or as negligible or trivial or whatever in the terms of the various framers of recent legislation.

I don't think that the problem is restricted to the migration of small amounts of material from packaging stuff, but I think that is probably the most dramatic single illustration of it. The solution is not to erect a special statutory category of migrating additives. I think the right thing to do is to establish some congressional guidelines, even if only in legislative history, as to acceptability of risk, and then let's use risk estimation procedures as well as we can.

Mr. GOYAN. In a sense, one of the things that bedevils commissioners is what is usually referred to as "chasing analytical zero," or trying to get lower and lower levels, being able to determine them as we are.

The other side of that is also important to understand, and that is that as you go to lower and lower levels, the confidence with which you can make a decision as to whether it really is the number that you have gotten becomes less and less; that is, the error in the determination becomes larger and larger rather shockingly fast, and thus we could be in the position of actually banning a foodstuff which was below the level that we wanted it to be, but we couldn't tell by analytical techniques, so it becomes quite complex.

The CHAIRMAN. Thank you, gentlemen

I have some other questions, but I am going to turn to Senator Quayle at this time and then to Senator Grassley right after Senator Quayle.

Senator QUAYLE. Thank you very much, Mr. Chairman.

I want to get set in my mind precisely what you are proposing. I understand from your response to Senator Hatch and also your testimony that you do believe that there should be some corrective remedial legislation to come out of this Congress to, in Dr. Kennedy's words, get us out of the regulatory quagmire that we find ourselves in right now.

You are specifically recommending some legislation. Am I correct in saying that, that we should do something legislatively?

Dr. KENNEDY. I carefully avoided saying when because I think that when one legislates depends a lot on political judgments about what is likely to emerge from a complicated process.

I have not been in close touch with the development of the proposals that have already been on the table, so I really cannot judge the propitiousness at the moment.

What I am telling you is that I think that, ideally, there should be some changes in this statute, and I think that since there is some momentum and some understanding, I think it should better be sooner rather than later. I have tried to characterize some directions in which I think those changes should go, but I obviously don't have specific legislative wording to offer you.

I do think that the general safety standard is appropriate. I think that there should be exceptions added to the Delaney clause to permit scientific demonstration of the inappropriateness of a particular animal test or of the negligibility of a particular cancer risk, and I think that the Congress should adopt a standard for negligible risk that can at least be generally understood by the agency and by others.

Senator QUAYLE. So if in fact the Congress would move forward with legislation—it would concern this Congress; we cannot go beyond this Congress.

Dr. KENNEDY. Sure.

Senator QUAYLE. You would draw the line, or relegate Congress indulgence, into putting some exceptions to the Delaney clause, a more appropriate definition of negligible risk, and am I also correct that you would do something with the definition of safe, or would you leave that basically as is?

Dr. KENNEDY. I think the general safety standard of the law is appropriate, but I do think that you should try to, in some definition section somewhere, establish a risk that you instruct the agency not to be concerned about.

Senator QUAYLE. Not to be—pardon?

Dr. KENNEDY. Not to be concerned about.

Senator QUAYLE. All right. Dr. Goyan, do you agree with that in a general sense?

Mr. GOYAN. Absolutely.

Senator QUAYLE. Let me ask this question. If we address these three general categories that you have talked about and grappled with, would this clear the decks on many of the aspects of the regulatory problem that you depicted confront us right now? Or would you say, Well, we've got these regulations under the old statute—I suppose your answer will depend on how precise and what kind of a new definition that the Congress comes up with—but I wonder if we would be adding to the problem. Is there a potential that we might be adding to the regulatory problem if in fact the Congress would move forward with a less than precise definition?

Your definition or your suggestion of changing "reasonable certainty" to "estimated incremental cancer per 1 million population," something along those lines, is getting fairly technical, and I can just imagine witnessing a discussion on the floor of the Senate about this particular aspect. When we start getting that technical, Congress, in setting policy, is liable to be far more general. I am just wondering if we might not be adding—is there a risk that we would be adding to the regulatory burden, or would this really clear the decks in many respects?

Dr. KENNEDY. In my judgment, Senator, it would help a lot more than it would hurt. Any expression, even through legislative history, of what congressional understanding is of the levels of risk that are acceptable is going to be valuable to the agency.

I think it is a very tough one for the Congress to grapple with, and I quite understand your discouraged scenario about what that debate would sound like. But all I can say, Senator, is better you than me. [Laughter.]

Please understand what I am saying.

Senator QUAYLE. That is what that Wall Street Journal editorial said.

Dr. KENNEDY. What the Commissioner has to do, if you folk do not grapple with that problem, is to justify to you what he has done administratively without guidance. And, believe me, by the time I get up and testify, as I did 43 times during the 27 months I had that job, you've got a pretty good idea what is acceptable because you've got a lot of constituent mail on it, after the fact. I want you to come to grips with it before the mail comes in the door.

Mr. GOYAN. Basically, what we are asking is, we want to find a way of defining insignificant risk for the Commissioner.

Senator QUAYLE. Insignificant risk for the Commissioner. We want insignificant risk for the Congress.

Mr. GOYAN. I understand that. [Laughter.]

Senator QUAYLE. You know, I think that what you have just outlined there is really a rather catch-22 situation and perhaps a comfortable situation that Commissioners find themselves in, present-day commissioners and the Congress, because the laws that we have right now allow the Commissioners to say, Well, we cannot have any risk at all when we get down to the Delaney, absolute zero; but if we find it, such as with saccharin, we always know we've got a safety valve because the Congress is not just going to let this happen. They will get constituency pressure. We can sit there and just blame it on FDA and the Commissioner and say what a bunch of lousy administrators and regulators we have in this area, overzealous, who don't know what they are doing, and we will just pass a ban.

On the other hand, you are very comfortable in making decisions because you can say, Well, when I get down to making this decision, I know that if I make one that is not going to be acceptable politically, this law is very rigid and I have a little bit of discretion, and I will go ahead and make that knowing full well that the Congress, in fact, may bail me out.

If we are in that kind of situation—well, it is you, Senator, rather than us—I think that is where we are, and I am trying to get off dead center there.

Dr. KENNEDY. I understand.

Senator QUAYLE. And I wonder whether you might be able to give us some encouraging advice on how do we get off dead center. You pointed out, going back to that Wall Street Journal editorial, that there is really a misunderstanding there, but in the public arena, if something comes, we don't want to be the fall guys; it is going to be you downtown. That is the target. We get this interplay going and nothing happens except for more and more testimony, more and more regulation, more and more hearings, more and more oversight, and it is very frustrating.

Dr. KENNEDY. I think you have made a very good case the other way, and let me tell you where I think it is likely to settle out.

I think it is likely that the Congress and the administrative agency will always be sharing those hazards to some degree, because the Congress cannot possibly write an absolutely rigid, or even a fairly rigid, prescription about what the acceptable risk is. I didn't propose that in my testimony and would not dream it to be possible.

But what we have now is the agency working without even any vague congressional indication of what ballpark acceptable risk falls in, and that I think is unfortunate. What I would like to see you do is at least address the problem seriously enough to give, in the legislative history, an indication about acceptable levels of risk with which the agency can then move forward.

You will have plenty of chance, I think, to share blame if something goes wrong. But at least then the agency has something at which to aim risk assessments and regulatory actions based on those risk assessments.

Mr. GOYAN. And absent that, you invite continued creativity on the part of the agency in a way that can only lead, I think, to more and more problems for everyone.

Senator QUAYLE. Absent statutory change, we can have, and we are going to have, some very significant and substantive hearings these next 3 days, and as I pointed out in my earlier statement, I think the groundwork by Chairman Hatch has been very, very good this time. It is very objective and everyone is going to have a say.

But absent statutory change, to get a message or to get FDA a position to hang its hat on or to get what we want to see, perhaps a more reasonable interpretation with less regulation, since that would be desirous, what would it be? Would it be reports? What are we really talking about? Aren't we talking about a statute? Aren't we talking about actual legislation?

Dr. KENNEDY. Oh, yes, I think you are, because you have to have something to attach a view to. What I am saying is, even if the statute that you actually produce is silent in its own language on that point, at least if there is a solid legislative history that trails after it and can be used, that is some help.

Mr. GOYAN. I wonder if I might just add to that.

If the Congress were to come forward with a bill that did speak of a reasonable certainty of insignificant risk but then, in the legislative history, indicated that an insignificant risk would appear to be something of the order of one to a million over a lifetime, that would be a very clear mandate to the agency.

Senator QUAYLE. Are you saying to me that, really, if we would in fact endeavor to change this law, the actual statutory changes would be very, very minimal, and that what would be far more significant would be, as you refer to it, the legislative history, the intent, the discussions that led up to Congress enacting this legislation?

Is that far more of a substantive basis of what we are talking about? And then, in a statutorial basis, we are talking about a rather vague—as you pointed out, Dr. Kennedy, we ought to make these changes, but you are not, at this particular time, going to make any specific recommendations for changes—is that what we are talking about? Is that where we are?

Dr. KENNEDY. I think that probably understates it a little, Senator. We have just been concentrating our discussion right now on the standard of safety, which I happen to think is the most important one, and I think if you did nothing else, that would be indeed a useful thing to do.

But there are a number of other changes that can be made at the same time, some of which I have alluded to in my testimony, and I think if you have a chance to spend the time holding hearings and developing momentum for a statutory revision, it ought to be a thoroughgoing one.

Senator QUAYLE. Let me just ask you, what momentum do you think is necessary to carry a piece of legislation through?

Dr. KENNEDY. Well, I think the existence of preceding attempts and the education that those have produced—you have a previous Senate bill; you have two previous House bills in the last 2½ years; you have an administration working group proposal based on some of the earlier proposals that originated in the Senate and separately in the House. Those have had hearings and criticism.

All of the interest groups, industry and consumer groups, have paid very hard attention to this issue over the past couple of years. So everybody is pretty far up the learning curve. You have a lot of players around who have thought about particular kinds of changes, have debated them, and remember the terms of the debate. That is what I mean by momentum.

This is a highly technical, complicated law, and the body of regulation built on it and the experience of the agency that is built on it are complicated. That has been distilled into some proposals, and the points of difference are well located. That is something to build on, in my judgment.

Mr. GOYAN. I think it would be a shame if you don't.

Senator QUAYLE. A shame if we don't do something?

Mr. GOYAN. Yes.

Senator QUAYLE. Do you see any future decisions on additives that the FDA may be making in the near term that might have an input into momentum? You know, if you get the public riled up, that is certainly momentum, rather than discussing it in the various groups and on a technical basis. But do you foresee any decisions in the near term that may add a little bit to this momentum?

Dr. KENNEDY. Senator, my poor brain only has room for a limited number of things, and I find that all of the spaces that were previously occupied by food additives have now become filled with indirect cost recovery and related matters. [Laughter.]

Senator QUAYLE. How about indirect cost recoveries in the future?

Dr. KENNEDY. No, I haven't kept track of pending proceedings within the agency and wouldn't really be knowledgeable enough about them to comment.

Mr. GOYAN. I wouldn't, either. All I would say is, I certainly hope not, because I don't see that simply having the agency beaten up once again over making what is perceived to be a silly decision would not achieve very much.

Senator QUAYLE. Let me ask one final question, Mr. Chairman, and then I will yield.

This Monsanto case and the de minimis exception were mentioned earlier. Would that apply to the Delaney clause?

Mr. GOYAN. It did not in that particular situation.

Senator QUAYLE. I know it did not in that case, but could it? Could the de minimis exception apply to the Delaney clause?

Dr. KENNEDY. Well, a Federal judge can do quite a lot of things.

The CHAIRMAN. Some of them do.

Dr. KENNEDY. I would think one could surely do that. I think that in your own crafting of the statute, whatever definitions of minimal or trivial or negligible you wish, you can and should apply by definition to both.

Mr. GOYAN. I would only add to that that Judge Levinthal essentially declared the second law of thermodynamics to be inappropriate or unenforceable in some fashion in his decision, so if he can do that, he certainly could overturn the Delaney clause.

I would add to that, however, that you also ought to look at the benzene decision that was handed down by the Supreme Court, because I think there are some precedents there that also obtain in this case.

Senator QUAYLE. I bring that out because I think that we will probably hear at some time during the testimony that there is no real reason—that argument will be made—to change the Delaney clause because of this Monsanto decision that did not apply to the Delaney clause, but the theory of de minimis could, in fact, be applied to the Delaney clause. So we really don't have that zero risk or the absolute factor that everybody says is too inflexible.

I think we are going to hear that, and that is why I asked the question.

Dr. KENNEDY. No; I think you need to make that change legislatively if it is to have any carrying power.

Senator QUAYLE. I thank both of you very much.

Thank you, Mr. Chairman.

The CHAIRMAN. Thank you, Senator Quayle.

Senator Grassley.

Senator GRASSLEY. Dr. Kennedy and Dr. Goyan, you have both been very busy as public servants and you now are very busy in the private sector. I want to thank you for taking time to present testimony at this hearing. You have had a lot to do with this law and can be very helpful in analyzing the need for change.

I think my questioning goes more to the administering of existing law. Any changes would perhaps follow some legislation similar to that which former Congressman Wampler has sponsored in the House. That has been tossed around for a while because we are wrestling with whether or not changes are necessary to the law or whether the law should be left the same, while making it more administerable.

I believe that I made clear in my opening statement why I have been critical of the FDA, particularly in its handling of the nitrite substance. My major point is that unjustified action cannot be undertaken by the FDA to the detriment of thousands of small processors and producers who work very hard to make sure that their products are safe, nor is it fair to our consumers who will become increasingly confused or misled by our food safety policies.

I do not mean to imply that after a long period of time of considering a difficult situation, Dr. Kennedy, that you had a very easy job at that particular time, even though at that particular time I was highly critical of what you did. I am more appreciative now of the area of legislation you had to operate in.

I am especially appreciative this morning of your comments in support of changes in the law. However, I am still left with some concerns on how we can avoid a repeat of anything like the nitrite issue or anything similar to it.

Specifically, Dr. Kennedy, how do you view what went wrong with the system in the nitrite situation now, upon reflection on the situation, 3 or 4 years later, depending on whether it was 1978 or 1980? I know you resigned soon after 1978.

Dr. KENNEDY. I promise you, Senator, the relationship was not causal. [Laughter.]

Senator GRASSLEY. I appreciate that, and I didn't mean to imply that, either.

Dr. KENNEDY. Well, you present an interesting challenge to me, Senator, as you well understand. I don't wish to come off as sounding at all defensive about the nitrite matter. I think that to the extent that I or anybody else in that job makes mistakes, the best possible thing we can all do is try as objectively as we can to learn something from those mistakes.

I have asked myself a number of times exactly what might have been done differently with respect to nitrites and with respect to the news that arrived in the form of that study. I have to tell you honestly that, although there are a few things I think I could have improved on, and although other people could perhaps have handled them better, I don't think there is either a specific statutory revision or a specific procedural or administrative change in practice that would make that particular event or that class of events impossible to occur again.

Let me, if I may, try to explain that a little more carefully. I cannot envision how you can charge a regulatory agency to proceed other than by giving it a congressional view about the acceptability or nonacceptability of risk, a criterion on which to judge the magnitude of that risk, and then some discretion as to looking at scientific results.

The result that the agency got with respect to nitrites was, in the judgment of a lot of people who looked at it, a quite convincing one. I happen to think the jury is still out on exactly how right or how wrong it was, although I am well aware of the changes that have occurred in some important conclusions of that study.

But let us assume, for the sake of argument, that it is just plain wrong. Every once in a while, a piece of good science, done in a good place by good scientists, is going to be wrong; there isn't anything you and I can do to prevent that, and there is not, I think, anything that you can build into an agency peer review or committee process that will prevent that. No peer review committee was going to take two pathologists and 6 months to review those slides; and if you made that an institutional requirement for every toxicological study, you would congeal not only the agency but the process of doing toxicology in the country. There just is not that much talent around to do it.

So I think it is just inevitable that any procedure in which the Government is asked to perform risk evaluation based on science is going to yield an occasional false positive.

We could debate for a long time whether there should be more damping built into the system so that there is not as rapid a response—so that the Commissioner was, let us say, required to hold something for a period of time. You might have delayed some of what you understandably regard as the bad effects of that decision by some delay that might be part of a statute, but I don't think you can eliminate the possibility of being given a result that indicates a pretty high probability of risk, and then being caught in the dilemma of either delaying acting on it and putting people at risk or acting too quickly and putting other people at risk. That is almost always what it boils down to.

I am not sure that is a very thorough answer to your question, but it is the best I can do, I think.

Senator GRASSLEY. Well, it may be difficult to answer, but I think your candid response and particularly your experience in this area ought to be taken into consideration by us as we consider any suggested changes.

But I would still like to go into just a little more detail, if I could, and more specific questions that might deal with further refinement of this.

What would be your view as to the merit in having results of a contracted study reviewed and evaluated by a committee of well-qualified scientists before decisions are announced? Now, you already spoke to the fact that it is obviously going to take time. But beyond that, do you see merit as a regular procedure or at least on an ad-hoc basis under certain circumstances?

Dr. KENNEDY. I think that could be done, and often is done informally in many agencies. We certainly sent the study and a draft of our regulatory response to it to a number of scientists in government and out; but it was an informational process, and it did not embody a particular peer review committee or advisory committee.

There is an alternative entirely to doing contracted studies in this particular way, and that is represented by a new institution called the Health Effects Institute, with which I have been involved, it is an organization supported both by Government and industry, and itself contracts and peer reviews the research.

There are some advantages in having that kind of arrangement because not only does it open up a new set of researchers on a particular topic to Government work, but it also contains a mechanism for peer reviewing the study before the Government gets it.

There are a variety of institutional possibilities of that sort, and I am sure you and your colleagues will want to explore them. But I think that a regulatory agency with FDA's kind of responsibility is regularly going to find itself in the position of contracting at least some studies for highly specific purposes.

What I would say is that if there is to be a standardized requirement for peer review, the model of the drug advisory committees should be the one that is used.

Senator GRASSLEY. You anticipated my second question, so I will go on to the third one.

Is it important to have these reviews conducted early in the review process, or can they wait and more or less serve as the court of review later on in the process?

Dr. KENNEDY. I would not call them a court of review, and I think it is very useful to have them have a more or less continuous observation of the process rather than only come in at the end. I think that it is often very useful to have judgments about design and execution as well as about conclusions.

Senator GRASSLEY. Do you think that a contractor for a study should announce his conclusions before the contracting agency has had an opportunity to review the report of the study?

Dr. KENNEDY. It depends on whether you are talking about contract review or whether you are talking about just the thing done by project monitors to be sure that the terms of the contract are fulfilled, or some kind of peer review.

Senator GRASSLEY. I would mean with the substance of the report as opposed to whether or not the financial aspects of the contract are being met and whether, in a timely manner, it is progressing, the quality of it, and proceeding. I am talking about the end product.

Dr. KENNEDY. Yes, I understand. I think that that would not be a wise provision, and I say so, Senator, because a lot of the institutions that will provide the best scientific work of this kind are the research universities of this country. Almost all of them have the same kinds of policies mine does, namely that faculty members who do research supported by whatever sponsor are free to publish those results. They are free to publish the results of their own work without being required to wait more than a rather short interval for prepublication agency review.

We have done battle with some other Government agencies over that principle, and we think it is pretty important. When I say "we" now, I have got my university hat back on. I would want to retain for the use of FDA and other Government regulatory agencies that important storehouse of fundamental research talent.

Senator **Grassley**. Lastly, and just taking a little different perspective of the overall issue now as opposed to zeroing in on the administration of this law or any new law, the problem I see if we have either this bill or any other law effectuated, and we say that—let's say that we have banned nitrites, and by banning nitrites we have banned one of the causes of cancer. I think we leave a misimpression with people that we have solved a problem dealing with nitrites and cancer, whereas the meats that it would be banned from are only a small portion of the nitrites that are with human beings constantly—whether it is produced in the body itself, whether it is produced naturally in other foods that we eat.

How do we deal with the problem if we are trying to approach a risk-free society—and there are some people trying to approach this, or a risk-free diet, whatever the case might be—and we have a Government agency that might say implicitly that we have taken care of a problem, and really, we have not? Do we go on, then, to tell people about all the problems we have with all the other nitrites that are being consumed, being made right within the human body, just by the natural process of living?

Dr. **Kennedy**. I think we are going to encounter a number of situations, regardless of the risk standard. I mean, suppose we adopt what you would consider a more reasonable risk standard. We will still find ourselves regulating some substances that occur naturally and that we get unavoidably.

Let's suppose that there is a substance 50 percent of which we receive by controllable routes and 50 percent of which we receive by uncontrollable routes. If it is really a carcinogenic substance, even if we can control only half of it, we would presumably wish to do that.

Your question is, do we come clean with people about the part that we cannot control? I think the answer is, yes, we do. We will probably pay some social cost for that in the form of raised anxiety, and I do not know how to get around that.

Senator **Grassley**. You would deal with this in the particular instance of your ban or would you desire to completely phase out—which you could not do—nitrites?

Dr. **Kennedy**. Yes. The contribution of other sources of nitrite was dealt with in the regulatory proposal that you have probably seen.

Senator **Grassley**. All right, but how did you deal with the public's perception of just the announcement that nitrites could and would be banned?

Dr. **Kennedy**. My recollection of the public announcements is that we pointed out that nitrites occur in various foods and that we were concerned with only the part which was regulatable as a food additive use.

As you may recall, there was a good deal of scientific disagreement in other quarters about endogenously made nitrite and the amount of that and the amount that the part used in processed meats actually contributed as a percent of the total diet. So I think that there was substantial uncertainty left about that that nobody could make evaporate.

Senator GRASSLEY. Thank you, Dr. Kennedy. Mr. Chairman, I have no further questions.

The CHAIRMAN. Thank you, Senator Grassley.

Just let me ask you one or two more questions. You have been very patient with us, and your testimony has been extremely important for this committee.

Let me turn to you, Dr. Goyan.

Tomorrow, eight distinguished scientists will appear before this committee, and one of the issues that they have been asked to discuss is the meaning of risk when it is defined as, quote, less than one chance in a million over a lifetime, unquote.

Now, could you tell us your understanding of what this standard means and explain why you believe, quote, among most people there is an inherent feeling that such a level of increased risk is reasonable, unquote.

Are you in fact saying that a risk of one in a million is so low that no public health consequence would result?

Mr. GOYAN. Well, perhaps I am in danger of behaving in an anecdotal fashion as a former Commissioner, for which I would apologize up front.

However, in discussing these sorts of issues over a period of the last few years with a number of groups, if you tell them that you are talking about an increased risk of 1 in 1,000, people get very concerned; 1 in 100,000, they still show some concern. But there seems to be something a little bit magic about the one in a million. I confess, I feel it myself.

The important thing, though, is something I said earlier, and that is that by one in a million, we don't mean that you can then multiply that by the 200 million people in the United States and say that there will be 200 additional cases of cancer due to this substance over the next year. It probably means that we will never know—because there is usually no way of tracing back, because of the time difference between when you ingest a substance and when you develop the cancer—that there has been an increase. But all of our approaches to it are, as I say, so conservative that rather than being one in a million—although that would be our estimate—in most cases it is considerably less than that, and I really don't know what the difference is between 1 in 10 million and 1 in 100 million when you get down to that low a level.

The CHAIRMAN. Would you care to comment on that, Dr. Kennedy?

Dr. KENNEDY. Well, it is a very difficult world. We live in a society, as you well know, Senator, which will spend large amounts of resources to save the life of a particular identified human being who is in danger, but feels quite differently about the spending of resources to save a marginal expected life, identity uncertain, over the next year.

I think that people understand that certain risks that are taken voluntarily are very substantially larger than one-in-a-million risks, but I think that we also understand that people have a right to take those risks where they are patent and obvious and where they can understand them, even if they cannot estimate them quantitatively.

When we talk about the food additive laws, however, we are talking about involuntarily assumed risks. We are talking about people who cannot be expected to memorize all the hazards and cannot be expected to avoid substances based on those risks; rather, we are talking about a general standard that we would apply to the entire food supply.

So I think it is reasonable for us to be quite cautious and conservative about those risks, simply because we are asking people to assume them involuntarily.

I don't think there is anything particularly magic about one in a million/lifetime incremental cancer risk, but it is a number that strikes me, for the same reasons it strikes Jere, as a reasonable place to start.

The CHAIRMAN. Dr. Kennedy, in your testimony, you state that the Delaney clause is undesirably inflexible in two different ways. First, it leaves no headroom for scientific progress. Second, by increasingly requiring agency action under conditions where the risks appear to be trivial, it invites public ridicule and disregard for the food safety laws more generally.

Now, could you elaborate just a little bit more on why the Delaney clause needs to be modified?

Dr. KENNEDY. Well, I think the chief casualty of its inflexibility really is that it doesn't offer any encouragement to those who would add substances to the food supply to go and find ways of demonstrating that they really are safe under the intended conditions of use.

I think a good law ought to offer people some incentive to reach rational and persuasive and scientific resolution of problems, and the present law does not do that. It simply says that if a substance is shown to cause cancer in animals or in people, then it simply should be banned from the food supply.

A rather small change would simply invite those who wished to add the substance to do studies to demonstrate that the studies which indicted it were done on an animal species that is not an appropriate model for human cancer in that organ or with that particular class of compounds; or would invite them to show, through the application of appropriate studies and risk assessment procedures, that in fact the amount of the substance that would actually occur under the conditions of use would present either no risk or a risk underneath the new standard that you set.

The CHAIRMAN. Thank you.

Dr. Goyan, would you care to comment?

Mr. GOYAN. I believe a regulatory agency can look almost anything except silly, and occasionally the Delaney clause puts the agency in a position where they are in danger of looking foolish and having the people essentially laugh at them, which is, I think, highly undesirable.

The **Chairman**. Well, I want to thank both of you for taking time out from what I know are very busy schedules and very important schedules, not only in your areas but throughout the country. We are very grateful to have you here today. Thank you for your testimony. Thank you for coming.

Dr. **Kennedy**. Thank you very much. Senator Quayle, Senator Grassley, thank you.

Mr. **Goyan**. Thank you.

The **Chairman**. Our second and final panel today on these food safety hearings consists of three expert scientists.

Dr. Frederick Robbins is president of the Institute of Medicine. Unfortunately, Dr. Robbins just had to leave to catch a plane. He has a commencement address to deliver in Illinois. But his associate, Dr. Elena Nightingale, is with us here today, and she will deliver his testimony and will answer questions pertaining to it.

I might add that Dr. Robbins served as chairman of the National Academy of Sciences Committee for a Study on Saccharin and Food Safety Policy. Dr. Nightingale served as staff director for the study, so she is highly qualified to read his statement and to testify and answer questions pertaining thereto.

Dr. Kenneth Fisher is the director of the Life Sciences Research Office of the Federation of American Societies for Experimental Biology.

We are delighted to have both of you with us today. If we could get you to come to the table, we will have Dr. Nightingale begin, and then we will finish up with Dr. Fisher.

We are sorry, Dr. Nightingale, that it has taken us so long to get here and that Dr. Robbins had to leave.

Dr. **Nightingale**. Thank you.

The **Chairman**. This is such an interesting subject and such a difficult subject that members of the committee, I think, felt very compelled to ask the questions that were asked this last hour and a half. We will turn to you now, Dr. Nightingale.

STATEMENT OF FREDERICK ROBBINS, M.D., PRESIDENT, INSTITUTE OF MEDICINE, NATIONAL ACADEMY OF SCIENCES; READ BY DR. ELENA NIGHTINGALE, SCHOLAR IN RESIDENCE, INSTITUTE OF MEDICINE

Dr. **Nightingale**. Thank you.

I am sorry that Dr. Robbins is not here, but I will do my best not only to read his statement but to answer questions insofar as I am able.

Dr. Robbins, who unfortunately had to leave to catch a plane, is president of the Institute of Medicine, and before that he was dean of the Case Western Reserve University School of Medicine and Chairman of the National Academy of Sciences Committee for a Study on Saccharin and Food Safety Policy. That study was completed in 1979.

His background, professionally, is in pediatrics.

I am a physician and a geneticist, and I was staff director for that study. I am currently a senior scholar in residence at the Institute of Medicine.

The National Academy of Sciences Committee that Dr. Robbins chaired issued two reports, one in late 1978 and one in early 1979. The first is a technical assessment of risks and benefits of the nonnutritive sweetener, saccharin. The second reviewed diverse aspects of food safety as well as risk and benefit assessment and the laws governing food safety.

The issues addressed in those two reports are as pertinent now as they were several years ago, as evidenced by these hearings. The issues include: One, determining and defining levels of risk; two, incorporating new scientific information into the regulatory process in a timely fashion; and, three, whether and how to consider health benefits.

A recent National Academy of Sciences report, "Risk Assessment in the Federal Government: Managing the Process," defined four stages of risk assessment:

> Hazard identification, which is the determination of whether a particular chemical is or is not causally linked to particular health effects;
>
> Dose-response assessment: The determination of the relation between the magnitude of exposure and the probability of occurrence of the health effects in question;
>
> Exposure assessment: The determination of the extent of human exposure before or after application of regulatory controls; and
>
> Risk characterization: The description of the nature and often the magnitude of human risk, including attendant uncertainty.

Certainly for foods as well as other substances, these steps in risk assessment are difficult to carry out. The content of the risk assessment report will be discussed later in these hearings, as I understand, so I will not pursue it further now.

It must be kept in mind that foods are mixtures of many chemicals, many of which are harmless if ingested in low amounts but, if ingested in large amounts, can cause disease or even death. Sodium chloride is an example. Some chemicals are essential nutrients in appropriate amounts and toxic in large quantities. Zinc is an example.

Therefore, it is impossible to have a food supply entirely free of "harmful" chemicals, since some of these chemicals in appropriate amounts are needed for normal metabolic function.

Furthermore, our current ability to detect minute amounts of certain chemicals means that foods previously thought to be "safe" are found not to be totally free of toxic chemicals. The goal of sound food safety policy is to minimize risks to health from foods, without unreasonably compromising availability, quality, and variety.

The problem of assuring a safe food supply has a number of complicating elements. One is that cancer, probably the most deeply feared of all diseases in this country, can take 20 years or more to develop after initial exposure to a carcinogen. The biological processes of cancer are still poorly understood, though we are learning more each day. The new information on oncogenes is an example,

Carcinogenic compounds are made by nature as well as by humans; indeed, we may manufature some within our own bodies. This was discussed just previously by Drs. Kennedy and Goyan with the example of nitrites. It is believed that nitrites are not potent carcinogens, if carcinogens at all, but in our bodies they may combine with other substances to yield nitrosamines, many of which are potent carcinogens.

A second element is that we now have scientific instruments that can measure traces of chemicals in our food supply as low as parts per trillion or less, but we do not know whether there is a level below which certain chemicals can no longer be considered carcinogenic or harmful. And there is a paradox here.

In times past, when only the grossest threats to the food supply could be detected, decisions were relatively simple. The demonstration of harm was usually so immediate as to remove any questions concerning the retention of offending substances in the food supply.

Now, however, because of our ability to detect minute concentrations and new laboratory procedures that can raise a suspicion of carcinogenicity, we are facing far more difficult social choices. Some substances in long use have come under suspicion. Moreover, new substances come into our food supply each year, and substances already in use are processed in new ways.

There are three main approaches to studying the safety of a food substance: Epidemiologic studies in man; laboratory studies of animals; and short-term tests using cell cultures or micro-organisms. For substances that have been in the food supply for a long time, clues to adverse health effects may come from epidemiologic studies which then need to be followed with studies in the laboratory. When seeking evidence of the safety—or adverse health effects—of a new food substance, investigators must rely on laboratory studies or animal models.

More specific information on recent advances in these three main approaches to studying the safety of food substances can be found in a series of reports; for example, the 1981 National Academy of Sciences Report on Nitrites and Nitrates, the 1981 Office of Technology Assessment Report on Determining Cancer Risks from the Environment, the 1983 study from the National Academy of Sciences on risk assessment I already mentioned, and the 1982 National Academy of Sciences study, "Diet Nutrition, and Cancer."

These studies and others, present summaries of our capabilities to determine safety and of the drawbacks of each of the methods in so doing. The testimony of Kenneth Fisher to follow also goes into this subject in more detail, so I shall not do that now.

Very briefly, epidemiologic studies may fail to provide evidence that a substance is hazardous unless the risk is very large or the disease very rare or distinctive. And animal studies involve extrapolation from high doses to low doses as well as from animals to people.

Studying the molecular structure of a substance is a help, as is doing a battery of short-term tests, mostly for mutagenicity. But these provide information about potential harm, mostly carcinogenicity, and are quick screens that serve only as warnings that further study is needed or that there is a suspicion of a harmful effect.

Doing all these kinds of studies can be complementary. If the direction of the result is the same, it would strengthen suspicion of harm. Nonetheless, for these and a variety of other reasons, there is likely to be great uncertainty, therefore, in assessing risks to health from foods.

The recent study, "Diet, Nutrition and Cancer," that I just mentioned, concluded—about food additives—that although the food safety provisions and, in many cases, the Delaney clause of the Federal Food, Drug, and Cosmetic Act prohibit the addition of known carcinogens to foods, only a very small proportion of substances added to foods have been tested for carcinogenicity according to protocols that are considered acceptable by current standards.

Moreover, except for the studies on nonnutritive sweeteners, very few epidemiological studies have been conducted to examine the effect of food additives on cancer incidence. Thus, in many cases, we do not know whether we are dealing with a major risk, a minor risk, or no risk at all, and as was pointed out earlier, it is not just the inherent qualities of the substance but the conditions of use that are of importance in determining which of the tests are appropriate and applicable to the human condition.

What characteristics should a system for regulating food safety have, given these complicated problems? In answering this question, the Committee for a Study on Saccharin and Food Safety Policy examined four substances. Saccharin was studied in the most detail; aflatoxins, nitrates and nitrites, and mercury, more briefly.

The committee recommended a conceptual framework to guide revision of laws governing food safety in order to foster a regulatory system that:

One, exerts continuous pressure for reduction in the overall risk from substances permitted in the food supply; for example, through encouraging the development of safer substitutes and requiring the use of safer substitutes when available, or reducing to the minimal level substances that are potentially harmful but have a benefit.

Two, is comprehensive and applies to all food substances equitably regardless of their route of entry into foods.

Three, distinguishes among risk levels based on estimates of both toxicity and exposure and assigns priorities among categories of risk. Particularly, irreversible toxicities—cancer, birth defects, or mutations—are to be considered of high risk if of appreciable frequency.

Four, allows a variety of regulatory and educational approaches in response to risks posed by food substances. The question posed by Senator Grassley earlier about communicating risks to the public is of importance here.

Five, allows the Food and Drug Administration the discretion to make judgments using expert analysis of scientific information and informed public opinion.

Six, provides greater scientific and other support for the Food and Drug Administration.

Seven, encourages the fullest expression of public opinion through education and active participation in decisionmaking.

Underpinning these general recommendations is the committee's strong belief that risk reduction should be the primary concern of the regulatory agency. However, in determining the kind of regulatory response to some substances, benefits, particularly health benefits, should also be assessed. Dr. Kennedy spoke to this point earlier. In general, we agree with what he said.

The American people are properly cautious about delegating regulatory discretion. A reasonable amount of responsible discretion, however, in a situation of such complexity, could avoid a far more burdensome and less effective set of rigid prohibitions, because statutes cannot deal in infinite detail with all possible eventualities.

These recommendations deserve some further comment. The committee assumed that assurance of a safe food supply requires effective regulatory action. It did not mean to weaken that. And the committee also felt that the Food and Drug Administration needed to be strengthened in its ability to meet its Federal responsibilities.

This does not necessarily mean that regulations need to be more stringent or more rigid. It does mean that the congressional mandate to the Food and Drug Administration should be clearly spelled out. FDA needs clear principles for action but also needs latitude about action on specifics so it can deal with new situations as they arise according to broad principles and objectives. It needs the ability to deal with new scientific information within a clear framework.

In addition, most of the committee felt that benefits, particularly health benefits, should be taken into account in regulating foods. However, it recognized that defining benefits, another topic of this hearing, is a controversial and complex matter.

People in the United States expect food to be safe, and generally that expectation is met. Protecting each citizen from food-related harm, however, if it is an absolute protection, may interfere with freedom of choice, highly valued in our society.

Protecting the safety of the food supply within the values of our society is an exceedingly complex and significant task. The interdisciplinary committee of the Institute of Medicine, chaired by Dr. Robbins, reached a remarkable degree of consensus, although, unavoidably, unresolved issues remain. Those who conducted the study viewed it as one step in a continuing process by which scientific knowledge of benefits and risks from foods can become deeper, and the links between this knowledge and reasonable policymaking can be made stronger.

The committee members were sensitive to the many scientific uncertainties and value conflicts embedded in issues of food safety policy. These hearings are also an important part of the continuing process of assuring a sound food safety policy for the American people.

Thank you.

The CHAIRMAN. Thank you, Dr. Nightingale.

[The following material was subsequently supplied for the record:]

Dr Robbins - the following are additional questions for you prepared by Senator Hatch

1) With a limit on resources, but with a seemingly infinite number of risks in the food supply, which risks should the Agency be concerned with?

2) What guidance should the Congress give the FDA in setting a standard of safety?

3) Do techniques exist which allow us to differentiate between risks that are very small and risks that are large?

4) Dr. Fisher, in your testimony you state that the Delaney Clause does not permit the exercise of judgement. Could you elaborate?

5) What factors, such as dosage level or metabolism, affect the relevancy of animal studies to humans?

6) What kind of evidence should the FDA have before it takes regulatory action against a suspected carcinogen?

7) A frequent criticism of the current statute is the FDA's lack of authority to balance both the risks and benefits of a food additive. Because of certain practical considerations, full risk-benefit analysis has rarely been advocated. What kind of benefits might appropriately be considered and under what circumstances?

8) During the past decade, FDA has used widely divergent ways of evaluating important and controversial food safety issues. On some occasions, it has handled these matters internally. On other occasions such as saccharin, it has requested that the matter be studied by the National Academy of Sciences. The Gras list review was conducted by the Federation of American Societies of Experimental Biology. With regard to cyclamates, the expert advice on the National Cancer Institute was relied upon. On certain substances such as red dye number 2, special consultants were employed, and on red dye number 40, a special working group was put together. What is the best way to handle peer review?

Isn't it widely recognized that such use of outside expert committees has, over the years, enhanced the credibility of scientific decisions made by the FDA?

Response to Additional Questions Prepared by
Senator Hatch for Dr. Robbins on Testimony
before the
Senate Committee on Labor and Human Resources
United States Congress
on
The Status of Scientific and Public Policy Issues
Related to Federal Food Safety Laws

Question 1

First, priority for attention should be given to those substances that are suspected of presenting the most serious risks. Criteria for determining the seriousness of the risks would be:

1. irreversibility, including lethality
2. chronicity (mental retardation would be such an example, as would cancer)
3. frequency of the effect--this relates to the pattern of use of the substances and the number of people adversely affected.

It often will not be possible to categorize substances according to severity of risk with any precision. However, it may be possible to make reasonable comparative judgements among different substances being considered.

Question 2

It seems reasonable for Congress to indicate to the Food and Drug Administration what degree of risk can be tolerated in the food supply. The Delaney Clause is an example of Congress's desire that no risk of cancer be accepted for a food additive. I would not favor an excessively precise definition such as one case of cancer in a million persons exposed. There should be leeway to take into account the kind of risk involved and whether or not there are significant benefits to a substance's use. It would be appropriate to indicate that the primary goal of regulation is risk avoidance, but to the degree possible, benefits should be factored into the equation.

One of the most important indicators of congressional attitude is the degree to which they provide the agency the resources to do its job by bringing to bear the best scientific evidence and judgement.

Question 3

Measures of severity of risk are often not precise. Evidence from human experience is obviously the best and this is never present to an adequate degree when one is considering a new substance. However, laboratory tests, including those in animals, can give guidance in order to make preliminary judgements.

Question 4

Question 4 is directed to Dr. Fisher.

Question 5

Some of the factors to be considered include:

1. dosage
2. method of administration
3. species of animal
4. comparative metabolism of the substance
5. precision with which the effect can be measured
6. method of caring for the animals
7. scientific validity of the protocol.

Question 6

It is not possible to be absolute in setting criteria but I would suggest the following. Results of general types of short term tests for mutagenicity and carcinogenicity and tests-- both short term and long term-- in two species of animal. However, what kind of regulatory action to take would depend also on other factors including evaluation of human data, strength of effect, whether the substance has benefits, how widespread its use is, which populations use it, etc.

Question 7

I would oppose insistence upon a formal risk/benefit assessment since benefits are often hard to substantiate and quantitate. However, if and when benefits are considered, I would suggest placing primary emphasis on health benefits.

Question 8

There is not necessarily a single "best" way to conduct evaluations. I would favor the free use of outside experts to assist in specific problems. The proposal made in the recent report of the National Academy of Sciences's committee on instutitional mechanisms for risk assessment seems to offer an excellent mechanism for guiding a risk assessment process.

I do believe that the use of independent advisory groups enhances the credibility of the agency.

The **Chairman**. Dr. Fisher, we will turn to you at this point.

STATEMENT OF KENNETH D. FISHER, Ph D., DIRECTOR, LIFE SCIENCES RESEARCH OFFICE, FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY

Mr. **Fisher**. Thank you, Mr. Chairman.

Let me express our sincere appreciation to you and to members of the committee and staff for the opportunity to present an overview of several issues involved in food safety from the perspective and the experiences of the Life Sciences Research Office.

I would like to say that I am accompanied today by my associate director, Dr. Frederic Senti, who has also been involved in many of these activities.

The federation was formed in 1912 and consists of seven major biomedical societies. Its membership includes approximately 24,000 scientists in this country and abroad whose expertise is in the area of biological and medical sciences.

One major purpose of the federation is to disseminate information on the results of biomedical research. The Life Sciences Research Office was established in 1962 to apply research results to specific issues in biology and medicine confronting Federal agency administrators.

From 1972 to 1982, the Life Sciences Research Office performed an extensive review of the generally recognized as safe—or GRAS—food substances for the Food and Drug Administration. This review of GRAS substances was conducted by an 11-member committee known as the Select Committee on GRAS Substances. In addition, the office has conducted a number of specific studies related to toxicology, nutrition, and food safety for various Federal agencies.

We were pleased to receive and accept the committee's invitation because of the Federation's continuing interest in scientific aspects of food safety. It is our hope that this scientific overview, based primarily upon the experiences of the Life Sciences Research Office and the Select Committee on GRAS Substances, will be a constructive contribution to the hearings.

At this point I would like to state for the record that the federation has not developed a formal policy statement on food safety legislation per se, nor does it expect to do so.

Also for the record, we have provided additional written information concerning the federation, the Life Sciences Research Office, and, more importantly, two major reports of the Select Committee on GRAS Substances about the GRAS review process.

The **Chairman**. Without objection, we will put all of that in the record.

Mr. **Fisher**. Thank you.

[No additional materials were forwarded for incluson in the record.]

Mr. **Fisher**. In the brief time available, I wish to comment on several aspects related to major issues in food safety as we perceive them.

First are the advances in food science and toxicology testing. During the past 30 years, the number and diversity of foods available to the public and considerations of food safety have expanded rapidly. In the early 1960's, little attention was paid to possible mutagenic effects of substances. Today mutagenicity testing is commonplace. A decade ago, little concern was voiced about the effects of food ingredients on nutrient bioavailability. Today it is an important consideration.

Carcinogenicity testing has become standardized, even though the applicability of certain types of carcinogenicity testing to carcinogenesis in man remains an unresolved scientific issue.

Teratogenicity testing is becoming accepted practice in hazard evaluation. Increasing notice is being paid to behavioral effects of the consumption of certain substances in foods.

During the period of the GRAS review, the use of microbial and other short-term tests for mutagenicity testing increased markedly. Additional short-term tests are now being developed and are being used as predictors of potential genotoxicity. These include both in vitro tests employing bacteria, fungi, mammalian cell lines, and in vivo mammalian test systems as well.

Although some scientists believe that a battery of these tests may eventually substitute for carcinogenicity testing in mammals, this may be unlikely. At the present state of their development, positive results from these short-term tests are considered mainly as indicators that additional scientific study might be conducted.

Similarly, there is ample reason to believe that food scientists will continue to develop new forms of foods which will provide more bioavailable nutrients that are acceptable to consumers and that make a wider use of sources of nutrients and calories. Similarly, there is every indication that toxicity testing will continue to evolve more precise techniques for measuring biological effects of substances.

For these reasons, legislation on food safety should be sufficiently flexible to permit the regulatory process to reflect ongoing advances in toxicology and food science.

The second point relates to advances in the identification of toxic substances. Without belaboring the point, because other witnesses have spoken to this, it seems clear that our analytic capability to identify specific substances in minute quantities will continue to develop and will increasingly detect both natural and synthetic chemicals not now known to be present. Food safety legislation should permit appropriate regulatory responses to issues arising from continued advances in analytical capabilities.

Third is the issue of advances in our ability to extrapolate risks to human health posed by toxic substances. In food safety, just as in other issues of human safety resulting from exposure to substances, practically all toxicological evaluations must address the problem of relating animal test data to probable effects in humans.

Experimental biologists are constantly striving to improve animal models which are most appropriate metabolically in terms of their similarities to the human being. Scientific advances now permit useful correlations of subtle indications of toxicity in animals with a number of variables. Animal models having characteristics which are similar to those of humans can be selected. Yet there are always other controllable factors which may affect the outcome of experiments. Despite critical attention to a host of variables, results with any given animal model may not be entirely applicable to human conditions.

For these reasons, experimental results with animal studies require careful analysis and interpretation by knowledgeable scientists. Based upon the information available during the GRAS review and its interpretation by the select committee, it appears that animal data most useful as predictors of human response are those data that are obtained from experimental animals or a combination of experimental animals for which the pharmacodynamics and pharmacokinetics of the test substance are as close as possible to those known to occur in man.

In this regard, it should be noted that the select committee also suggested that observations on human subjects provide the most meaningful data for estimating human risks associated with food ingredients. Clearly, ethical considerations limit the performance of such experiments on man, and appropriate animal experiments must be completed before studies can be performed in humans.

The fourth issue is the definition of safe. Absolute safety is an ideal toward which most individuals concerned with food safety aspire. Thus, the select committee operated with the stipulation that credible evidence of, or reasonsable grounds to suspect, adverse biological effects had to be present in whatever information was available before their scientific opinion on a potential health hazard was to be made.

This basic principle is the reverse of the premise for the approval of new additives. This dichotomy of approach for GRAS Substances, on the one hand, and food additives on the other, is one major reason why the Select Committee on GRAS Substances called for instituting uniformity in scientific evaluation of the safety of substances added to food.

Many knowledgeable individuals have attempted to define safe in the context of food safety as, the "absence of harm" to human health. This may be as accurate a statement as can be made. However, it is not possible to define "safe" scientifically. The expression "absence of harm" suggests zero risk, a situation which can be approached but never achieved.

There is a definition of safe in the Code of Federal Regulations, and there may be good and sufficient reason why a similar definition of safe has not been included in the act up to now. Because a multiplicity of interpretations can be placed upon words, identifying something as "safe" has involved, and continues to involve, a series of value judgments based upon the interpretation of the best available information.

Stating that, for regulatory purposes, the appropriate agency or department shall determine from an evaluation of all scientific or other information what might be considered safe may be a rational approach in terms of legislative recognition of the complexity of this issue.

Fifth is the Delaney clause, about which we have heard a considerable amount of discussion. This discussion mirrors the great public concern related to cancer. Of particular scientific concern is the language of the clause which states in part that no additive shall be deemed to be safe if it is found to induce cancer when ingested by man or animal or is found, after tests which are appropriate for the evaluation of safety of food additives, to induce cancer in man or animal.

This legislative all-or-none absolutism presents difficulties when applied in the real world. The clause makes no distinction among the type of chemical or physical agent involved in cancer induction, nor does the law, as currently written, take into account evolving knowledge of carcinogenic processes.

High dosages are employed in long-term animal studies to reveal toxic potential, if any. This design maximizes the chance of tumor induction. Such protocols are highly refined and are well organized, and tests are conducted with appropriate care and scientific acumen. While they exemplify the best efforts of science, extrapolation to situations analogous to human consumption requires the application of reasoned judgment by knowledgeable investigators. The appropriateness of such tests is a matter of continuing discussion.

In its recent review on insights on food safety evaluation, the select committee recommended modification of the Delaney clause to allow for necessary flexibility in the interpretation of scientific and medical data by knowledgeable experts and responsible health authorities.

An additional issue is the consideration of benefits of food ingredients in food safety decisions. Except in the case of certain vitamins and minerals, benefits were not considered in evaluating the health aspects of GRAS Substances, and no attempt was made to obtain the analysis necessary for arriving at benefit/risk assessments.

However, relating benefits to risks on considering matters of safety has become prevalent in recent years. While a benefit/risk assessment of food ingredients is not feasible as an exact mathematical relationship and its application in specific cases may be difficult, the concept does have value with respect to food safety in cases where health benefits can be compared with health risks.

Finally, the role of independent expert review of scientific information in food safety is a major point. In the past two decades, a number of efforts of external scientific review and evaluation have been quite successful and appear to be highly regarded both by the scientific community and the general public.

These include the several working groups on chemical carcinogenesis of the International Agency for Research in Cancer, the Federation's Select Committee on GRAS Substances, and the several committees of the National Academy of Sciences that Dr. Nightingale has mentioned.

Clearly, evaluation panels can be constituted by industry or consumer groups. Similarly, Federal agency scientists do and can conduct intramural safety evaluations. But it is an important distinction that independent evaluations of scientific data by evaluation panels constituted by organizations of acknowledged scientific reputation, free of vested interests in regard to proposing or opposing the use of a substance in food, do avoid unnecessary controversy and increase public confidence in subsequent Federal agency decisions concerning regulatory matters.

Scientific panels independently constituted by organizations whose major purpose for existence is science itself appear to be the most acceptable means for obtaining unbiased evaluations of scientific information. Should the current law be modified, consideration should be given to delineating more clearly the separation of scientific evaluation by independent scientific organizations in cases where such review is deemed to be necessary and the subsequent regulatory decisions that would be made at a later date by Government agencies.

Senator Hatch, this concludes my oral presentation. A more detailed presentation of these remarks is contained in the written submission.

Again, I appreciate the opportunity to submit this information on food safety and would be pleased to provide any additional information we can.

[The prepared statement of Dr. Fisher follows:]

CORRECTED COPY
June 10, 1983

PREPARED STATEMENT

of

Kenneth D. Fisher, Ph.D., Director
Life Sciences Research Office
Federation of American Societies for Experimental Biology
9650 Rockville Pike
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to

Committee on Labor and Human Resources
United States Senate

for the

Hearing on Issues in Food Safety
June 8, 1983

I. INTRODUCTION

My name is Kenneth D. Fisher. I am the Director of the Life Sciences Research Office (LSRO) of the Federation of American Societies for Experimental Biology (FASEB). I am accompanied today by our Associate Director, Dr. Frederic R. Senti. Let me express our sincere appreciation to Senator Hatch, the Members of the Committee, and their staff for the opportunity to present an overview of the several issues involved in food safety from the perspective and experience of the Life Sciences Research Office.

Prior to joining the Life Sciences Research Office in 1968, I held several academic appointments that included experience in research and teaching in microbiology, plant pathology, and biological sciences. Since 1968, my professional experience has included a particular emphasis on nutrition and toxicology, but, more broadly, the environmental and life sciences. Since joining the Life Sciences Research Office I have been involved primarily in the analysis and evaluation of specific research topics and areas in biology and medicine.

Dr. Senti has been a member of the Life Sciences Research Office staff since 1974. At the Life Sciences Research Office, Dr. Senti has played a major role in the supervision of the staff responsible for the review of the Generally Recognized as Safe (GRAS) food substances. Prior to joining the staff of the Life Sciences Research Office, Dr. Senti served in a number of positions in a distinguished career spanning 33 years with the Agricultural Research Service of the United States Department of Agriculture.

The Federation was formed in 1912 and now consists of six major scientific Societies as corporate members, and a seventh Society as an affiliate member. Federation membership consists of approximately 24,000 scientists in this country and abroad whose expertise is in the areas of physiology, biochemistry, pharmacology, pathology, nutrition, immunology, and cell biology. The purposes of the Federation, as set forth in its constitution, are to bring together investigators in the biomedical sciences represented by the member Societies and to disseminate information on the results of research.

The Life Sciences Research Office was established in 1962 by the Federation as an arm of the Executive Offices designed to undertake analyses of specific issues and problems in biology and medicine confronting research program administrators in federal agencies. The Office provides expert evaluation of scientific issues utilizing ad hoc review of particular study topics conducted by knowledgeable scientists selected on the basis of their specific expertise in a scientific disciplinary area and their freedom from conflict of interest. Emphasis in LSRO studies is placed upon the development of a sound, scientific, factual basis for subsequent administrative decisions by the sponsoring organization.

During the period 1972 to 1982 the Life Sciences Research Office performed an extensive review of the Generally Recognized as Safe food substances for the Food and Drug Administration. When this review was undertaken, the Federation acknowledged a desire to lend its scientific resources and expertise to meet a specific societal need. The review of the GRAS Substances was conducted by an 11-member expert scientific panel known as the Select Committee on GRAS Substances. In addition to the experience garnered in this decade of activity, the Life Sciences Research Office has conducted and continues to conduct a number of specific studies which bear upon aspects of nutrition and food safety for the Department of Health and Human Services and other federal agencies.

We were pleased to receive and accept the Committee's invitation because of the Federation's continuing interest in the scientific aspects of food safety. It is our hope that this scientific overview, based primarily upon the experience of the Life Sciences Research Office and the Select Committee on GRAS Substances, will be a constructive contribution to these hearings. At this point I would like to state for the record that the Federation has not developed a formal policy statement on food safety legislation per se, nor is it expected that one will be developed. Also for the record, we have provided additional written information concerning the Federation, the Life Sciences Research Office, and two major comprehensive reports of the Select Committee on GRAS Substances. These include a paper entitled "Evaluation of Health Aspects of GRAS Food Ingredients: Lessons Learned and Questions Unanswered," published in October 1977, and the final report of the Select Committee on GRAS Substances published in December 1982 entitled "Insights on Food Safety."

II. PERSPECTIVES ON ISSUES IN FOOD SAFETY

In the brief time available, I wish to comment on several aspects related to major issues in food safety. These are: (a) advances in food science and toxicology testing, (b) advances in the identification of toxic substances, (c) advances in ability to extrapolate risks to human health posed by toxic substances, (d) the definition of "safe," (e) the Delaney Clause, (f) consideration of the benefits of food ingredients in food safety decisions, and (g) the role of independent expert review of scientific information in food safety.

A. Advances in Food Science and Toxicology Testing

When the first food safety laws in the United States were passed in 1906, questions related to fraud and adulteration of foods represented major reasons for passage of the federal law. It was clear that the government needed to control what went into food in terms of the safety of the product. In addition, government recognized the necessity for the control of processing food to insure that processing resulted in the preparation of a product that did not induce injury or disease and to insure that products met some minimum standards with respect to quality. Clearly, at that time, the individual family kitchen was the major source of prepared food products. In the 1950's, prior to the passage of the 1958 Amendment, food science had advanced considerably and a large number of substances were being added to foods for specific purposes including extension of shelf life, maintenance of quality, avoidance of microbial contamination, enhancement of flavor, texture, and color, as well as improvement in nutritional quality. By 1970 there were 7,000 commercial food items in supermarkets at any one time, and hundreds of new ones, many short-lived, appeared and continue to appear each year. Food preparation patterns in the United States were considerably altered. In addition to the availability of frozen, canned, dried, and preserved foods, as well as other pre-prepared and processed items, a significant proportion of food was consumed outside the home. For example, currently over half of all fruits and vegetables are purchased in processed form; more than 85% of the wheat flour milled is purchased as bread, bakery, or other ready-to-eat products; about half of potatoes reach the retail market in the form of chips, frozen french fries, and other processed forms; and about 70% of all sucrose consumed is purchased as an ingredient of processed foods.

Associated with the expanding spectrum of foods and food ingredients in the food supply, considerations of food safety were also expanding and the science of toxicology continued to advance and grow rapidly. In the early 1960's little attention was paid to the possible mutagenic effects of substances. Today mutagenicity is a major concern. A decade ago little concern was voiced about the effects of food ingredients on nutrient availability. Today it is an important consideration. Carcinogenicity testing has become commonplace and more standardized even though the applicability of certain types of carcinogenicity testing to carcinogenesis in man remains an unresolved scientific issue. Teratogenicity testing has evolved and is becoming accepted practice in hazard evaluation. Increasing notice is being paid to the behavioral effects of the consumption of specific substances in food. During the period of the GRAS review, the use of microbial tests for mutagenicity testing, such as those developed by Ames and others, increased markedly. Currently, additional short-term tests are being developed and are now being used as predictors of potential genotoxicity. These include both in vitro tests employing bacteria, fungi, and mammalian cell lines and in vivo mammalian test systems as well. Although some scientists believe that a battery of these tests may eventually substitute for carcinogenicity testing in mammals, this seems unlikely in view of the fundamental differences in DNA structure, variability in results, and the fact that some known carcinogens have little or no mutagenic activity. In the future, in vitro tests may play an increasingly important role in toxicological and other studies; however, at present knowledge is insufficient to justify extrapolation from in vitro systems alone to the whole organism. In vitro tests are not sufficiently developed for accurate prediction of human carcinogenicity. At the present state of their development, positive results from in vitro tests should be considered mainly as indicators that additional scientific study should be conducted by means of in vivo experimental evaluation.

There is ample reason to conclude that food scientists will continue to develop new forms of foods that provide sources of bioavailable nutrients, that are acceptable to consumers, and that make use of a wider range of sources of nutrients and calories. Similarly, there is every indication that toxicity testing will continue to evolve more precise techniques for measuring biological effects of substances. Thus food safety legislation should be sufficiently flexible to provide for inclusion of these expected changes in any mechanisms for scientific input into regulatory decision-making.

B. Advances in the Identification of Toxic Substances

Advances in analytical chemistry and their application to food toxicology are perhaps one of the outstanding contributions of science in the past several decades. Analytical techniques have been developed that permit the detection and identification of traces of substances in foods at parts per billion, parts per trillion, and even lower levels. That is, techniques such as gas liquid chromatography combined with mass spectometry, radioimmune assays, enzyme linked immunoassays, and fluorescent spectroscopy now allow us to identify extremely small quantities of substances that may be residues of prior treatments in foods, natural constituents in foods, substances that may migrate into foods from packaging or other food contact surfaces, or substances accidentally introduced into foods. Without belaboring the point, it seems clear that our analytical capability to identify specific chemical substances in minute quantities will continue to develop and will increasingly detect both natural and synthetic chemicals not now known to be present. Any modification of current legislation should permit appropriate regulatory responses to issues arising from continuing advances in analytical capabilities.

C. Advances in Ability to Extrapolate Risks to Human Health Posed by Toxic Substances

In food safety just as in other issues of human safety resulting from exposures to chemicals, practically all toxicological evaluations of substances must address the problem of relating animal test data to probable effects in humans. Scientists and expert committees, who have been concerned with the meaningfulness of animal test data in terms of human toxicity, have come to accept the necessity of qualifying opinions concerning the potential for human toxicity based upon studies with animal models depending upon the particular scientific question being assessed. Typically, greater concern for the certainty of a predicted result is associated with extrapolating risks of irreversible effects as contrasted to reversible effects, e.g., carcinogenicity vs. transient gastrointestinal effects in an animal. Toxicologists and experimental biologists are constantly striving to select animal models which are most appropriate metabolically in terms of their similarities to humans. Scientific advances now permit useful correlations of subtle indications of toxicity in animals with a number of variables.

Animal models can be selected having certain characteristics which are similar to those of humans, such as the rate of absorption of the test substance, blood levels obtained, tissue distribution, manner of excretion, and, more importantly, the rate and pattern of metabolism. Yet there are always other controllable factors that do affect the outcome of experiments such as the sex, health, and age of the animal, imposed stress, nature of the artificial diet, size and frequency of dose, route of administration, temperature, season, and altitude. Despite critical attention to a host of variables, results with any given animal may not be entirely applicable to human conditions. For these reasons, experimental results with animal studies require careful analysis and interpretation by knowledgeable scientists.

Another significant advance in testing methodology that makes animal data more useful for reaching conclusions concerning the safety of food ingredients for human consumption is the increasing ability to study the detailed metabolism of these substances. Such studies can provide insights into the mechanism of action of the substance at and below toxic levels in laboratory animals.

Based upon the information available during the GRAS Review and its interpretation by the Select Committee, it appears that those animal data that would be most useful as predictors of human response are those data obtained with experimental animals or a combination of experimental animal models in which the pharmacodynamics and pharmacokinetics of the test substance are as close as possible to those known to occur in man. Such studies include administration of the substance orally in food and include levels that might be considered characteristic of human dietary habits. Results obtained under such conditions can be extrapolated more confidently to humans.

However, where patterns of metabolism of substances in man are not known with certainty, the scientist is often faced with the dilemma of using an experimental protocol in an animal test model which may or may not mirror the human condition but provides a reasonable approximation of what might occur. In this regard it should be noted that the Select Committee suggested that observations on human subjects provide the most meaningful data set for estimating human risk. Such studies could be employed in those cases where animal data indicate no adverse health effects of a transient or irreversible nature. In calling for limited studies in humans on the basis of such information, a degree of confidence in animal testing is implied and their limitations underscored. Clearly, ethical considerations limit the performance of such experiments on man, and will generally exclude morphological and biochemical analysis of tissues other than blood and minute biopsy specimens (e.g., punch biopsy of skin or dental enamel). Appropriate animal experiments must be completed before limited studies can be performed in humans.

However, recognizing these restraints, a variety of human investigations are now practical and deserve consideration. Short-term studies of absorption, distribution within the body, metabolism, and excretion can be carried out given sufficient animal data to establish a "no adverse effect" level that could be used as a sound guide for determining a safe level of human ingestion during carefully monitored trials. Biochemical parameters may serve to identify potentially adverse effects before clinical manifestations become apparent. A food ingredient can be administered to a study group and amounts of the substance and metabolites appearing in blood and urine can be assayed. Modern analytical methods make possible qualitative identification and in some cases quantitative measurement of metabolic products resulting from extremely small administered doses. Such a determination of the pharmacokinetics of the substance and its derivatives in humans aids in the interpretation of animal data and in the design of further toxicity studies on the substance, if needed.

Two further comments in regard to our ability to extrapolate risks to human health posed by toxic substances may be in order. First, the Select Committee suggested that while in vitro tests may in the future play an increasingly important role in toxicological and other studies, knowledge at present is insufficient to justify extrapolation from in vitro systems alone to man. At the present state of their development, such tests should be considered mainly as indicators that additional scientific study by means of in vivo experimental evaluation should be conducted. Despite this admittedly conservative view, many investigators and commercial firms do use in vitro genotoxicity as a routine screening technique in the development of new products. Obviously, repeated positive results in such tests are going to have a greater impact on economic and managerial decisions related to production of a food or food ingredient by a firm than may be justified on scientific grounds alone. In a practical sense, while no extrapolation from in vitro testing to humans is scientifically justified, data on mutagenic effects from in vitro tests may result in the elimination of possibly toxic substances from consideration for human use. In this regard, in vitro genotoxic testing does contribute to safety of the food supply.

Second, given current public concerns with possible occurrence of carcinogenic substances in the environment and in the diet, the fact is that a conclusion of "carcinogenesis" is, on the one hand, either obvious and self-evident in an experimental system or in a human exposure situation; or, on the other hand, its characterization is a difficult judgmental matter. In the testing of new substances which may have application to uses in foods, this latter situation is most typical and requires both statistical considerations to determine the probability of carcinogenicity and an informed group of scientists to decide whether a "significant" and presumably reproducible effect was obtained. Even when this conclusion is reached, the "true" relevance of animal data to man continues to be subject to considerable debate.

D. Definition of "Safe"

Absolute safety is the ideal towards which most individuals concerned with food safety aspire. The central issue behind food safety is the definition of the level of socially acceptable risk and secondly, but of equal importance, being clear as to the procedures to be followed in arriving at that level.

The review of safety of GRAS substances should be considered in the perspective of the legal requirements imposed by the statutory language of the Federal Food, Drug, and Cosmetic Act as amended in 1958. Essentially, the Food and Drug Administration (FDA) has the burden of proof if a GRAS substance is to be declared unsafe for its intended use. Therefore, reasonable grounds must exist in order to question the safety of a GRAS substance and such grounds must be supported by substantive evidence derived from scientific data. Thus, the Select Committee operated with the stipulation that credible evidence of, or reasonable grounds to suspect, adverse biological effects had to be present in whatever information was available before the pronouncement of a potential health hazard was to be advanced.

This basic principle is, of course, the reverse of the premise for the approval of new food additives. In the latter case, there must be sufficient and credible evidence from tests specially designed for the purpose that demonstrates their safety before admission to commercial use. This dichotomy of approach for GRAS substances on the one hand, and food additives on the other, is one major reason why the Select Committee in their two treatises on the GRAS review called for phasing out of the GRAS list and instituting uniformity in evaluation of the safety of substances added to foods.

Many august bodies, scientific committees, federal agency groups, and knowledgeable individuals have attempted to define "safe." The thought that "safe" in the context of food safety implies absence of harm to human health is probably as accurate a statement as can be made. However, it is not possible to define "safe" scientifically. The expression "absence of harm" suggests zero risk, a situation that can be approached but never achieved. Science's ability to rigorously predict who is at risk, that is, who is susceptible, as well as the degree of risk that might occur, is inadequate in general and non-uniform at best. While there is a definition of "safe" in the Code of Federal Regulations there may be good and sufficient reasons why a similar definition of "safe" was not included in the Federal Food, Drug and Cosmetic Act. Because a multiplicity of interpretations can be placed upon words, identifying something as "safe" has and continues to involve a series of value judgments based upon the best available information, not all of which can be scientifically determined. For example: (1) What is reasonable certainty, or, perhaps, reasonable probability of safety? (2) To whom is there no significant risk? Can science identify potentially sensitive or susceptible population groups at risk prior to exposure to a substance which may affect human health adversely, beneficially, or not at all? (3) Many definitions include a phrase, "based on adequate scientific data;" how is this to be determined? Because each and every scientific review panel will evolve a consensus on what constitutes safety based upon data existing at that point in time, "adequate scientific data" becomes a constantly moving target. As such it is difficult to pinpoint but relatively easy to shoot at.

Recent attempts at more explicit definition have suggested that "safe" implies that scientific study can establish a point at which there are no adverse effects. No quantity of scientific investigation, no matter what its quality, can prove the negative. Consideration probably should be given to stating that for regulatory purposes the appropriate agency or department shall determine from an evaluation of all scientific and other elements what is to be considered "safe". This may be the only rational approach in terms of legislative recognition of the complexity of this issue.

E. The Delaney Clause

The Delaney Clause of the 1958 Amendment of the Federal Food, Drug, and Cosmetic Act is an issue of wide concern. When introduced in 1958, the Delaney Clause exerted a salutary effect in highlighting the need for special attention to one of the more dreaded diseases. This purpose has been realized and the food industry and government officials are well aware of the health concerns of the general public as reflected by Congress. However, implementation of the Delaney Clause is a legal matter. For example, it applies to food additives but does not apply to GRAS substances as they are legally another class of food ingredients. Thus the Select Committee's assessments were not constrained by it. Nevertheless, the existence of the Clause in the law resulted in discussions of its perceived importance in overall food safety during the Select

Committee's consideration of evidence for carcinogenicity. Of particular scientific concern is the language of the clause which states in part, "... that no additive shall be deemed to be safe if it is found to induce cancer when ingested by man or animal, or is found, after tests which are appropriate for the evaluation of the safety of food additives, to induce cancer in man or animal ...".

This legislative all-or-none absolutism presents difficulties when applied in the real world. The Clause makes no distinctions among the types of chemicals, or physical agents involved in cancer induction. Similarly, the law as currently written does not take into account evolving knowledge of carcinogenic processes. Current scientific evidence supports the concept of induction of cancer by several different mechanisms and provides considerable data showing that dosage, schedule, and route of administration as well as genetic capabilities, exert profound effects on the carcinogenic process.

High dosages employed in long-term animal studies are selected to reveal toxic potential, if any. The design maximizes the chances of finding an adverse effect, such as induction of tumors. Yet, these protocols may bear little semblance of reality to the actual exposures to which humans are subjected. The Select Committee was aware that such protocols are highly refined and well organized, and that generally the tests are conducted with appropriate care and scientific acumen. While they exemplify the best efforts of science, they do not yield useful answers without the application of reasoned judgment by knowledgeable investigators. The Delaney Clause as written does not permit the exercise of that judgment.

A second incongruity of the Delany Clause is that it applies only to direct and indirect food additives. Hence, if a substance known to be carcinogenic to animals is found to occur naturally in a foodstuff (e.g., aflatoxin) or is a GRAS or prior-sanctioned ingredient, the Clause does not prohibit it in food and the FDA must utilize other means to regulate its use.

In its recent review on insights on food safety evaluation, the Select Committee recommended modification of the Delaney Clause to allow for the necessary flexibility in the interpretation of scientific and medical data by knowledgeable experts and responsible health authorities. The Select Committee also suggested that inclusion of detailed technical criteria of safety for ingested substances in legislation is counterproductive to the assurance of food safety and should be discontinued.

F. Consideration of the Benefits of Food Ingredients in Food Safety Decisions

Benefit/risk assessment is useful in the evaluation of the safety of preventive and therapeutic agents because in such instances both benefits and risks are experienced by the same individual. Further, it is theoretically possible to express the benefits in terms of countermorbidity and the risk of the adverse side effects of a given therapeutic agent in terms of morbidity. For example, in the field of immunization against various illnesses, responsible medical experts have concluded that for the United States, tetanus immunization should be carried out because medical benefits outweigh medical risks whereas smallpox vaccination should not be performed routinely because the potential benefits from the prevention of a disease with a remote possibility of occurrence are less than the medical risks and possible costs associated with mass immunization programs.

A similar situation exists for food ingredients where a benefit to health from their use might be judged to outweigh a risk to health. Vitamins and other essential dietary ingredients fall into this category. A scientific evaluation panel can assess their benefit to the health of the consumer at a given exposure level and weigh the benefit against the risk of harm to the same individual. Health benefits to most individuals might be judged to outweigh risks in such cases, and those substances would be considered "safe" for human consumption even at levels having only a narrow margin of safety. Although there are potential risks from food fortification with iron, vitamin D, and vitamin A, the Select Committee believed such risks to be outweighed by the widespread public health benefits.

Except in the case of certain vitamins and minerals, benefits were not considered in evaluating the health aspects of the GRAS substances and no attempt was made to obtain the analyses necessary for arriving at benefit/risk assessments. However, relating benefits to risks in considering matters of safety has become prevalent in recent years. While a benefit/risk assessment of food ingredients is not feasible as a mathematical relationship and its application in specific cases may be difficult, the concept has value with respect to food safety in cases where health benefits can be compared with health risks.

G. The Role of Independent Expert Review of Scientific Information in Food Safety

The principles and general concepts of including independent expert scientific review of food safety issues by nongovernmental experts should be included in any revision of the current law. The details and logistics of how such scientific committees would function should be left to those organizations that are asked to conduct such reviews. A number of successful efforts of external scientific review and evaluation are highly regarded both by the scientific community and the general public. These include the several Working Groups on Chemical Carcinogenesis of the International Agency for Research in Cancer, the Federation's Select Committee on GRAS Substances, and several committees of the National Academy of Sciences that have addressed issues related to saccharin, nitrite, and interrelationships of diet, nutrition, and cancer. In each of these instances the evaluation panels were selected, organized, and conducted free of direction or specification by the sponsoring federal government department or agency. These committees were administratively within a separate organizational structure: specifically, a recognized scientifically constituted body free of vested interest or the appearance of vested interests by virtue of its scientific stature. These evaluation panels have been free to conduct their scientific reviews with the independence and objectivity of scientific judgment that such separation guarantees.

Evaluation panels can be constituted by industry or consumer organizations; similarly, federal agency scientists can and do conduct safety evaluations intramurally. But, it is an important distinction that independent evaluations of scientific data by evaluation panels constituted by organizations of acknowledged scientific reputation free of vested interests in regard to proposing or opposing the introduction or use of a substance in food do avoid unnecessary controversy and increase public confidence in subsequent federal agency decisions concerning regulatory matters. Should the current law be modified, consideration should be given to delineating more clearly the separation of scientific evaluation by independent scientific organizations and the subsequent regulatory decisions by governmental agencies.

In addition, consideration should be given to safeguarding the process that provides for panel members to be selected independently by the scientific organization. Such a process seems highly desirable, if not essential, to the credibility of any expert scientific evaluation panel. On the other hand, it is equally important that all segments of the public have an opportunity to nominate qualified scientists to such panels, and consideration should be given to inclusion of such stipulations. Because ad hoc expert panels that serve and advise federal agencies consist of scientists who devote only a fraction of their time to the panel's business, a full-time scientific and support staff to furnish support and mission continuity is vital. Appropriate guidelines must be established to assure that panel members and staff are free from conflicts of interest. Such considerations must be handled openly, yet discreetly, guarding carefully the invasion of privacy and the protection of public interest. Opportunities for input into the scientific evaluation process need to be provided to all individuals regardless of their vested interest or acknowledged bias.

In summary, scientific panels independently constituted by organizations whose major purpose for existence is science per se appear to be the most acceptable means for undertaking these activities and obtaining unbiased evaluations of scientific information that can be utilized to undergird subsequent regulatory decisions.

(NOTE: In the interest of economy, certain previously printed material accompanying Dr.Fisher's statement was retained in the files of the committee where it may be researched upon request.)

The CHAIRMAN. Thank you so much, Dr. Fisher, and you, also, Dr. Nightingale.

Let me ask you this. With a limit on resources, but with a seemingly infinite number of risks in our food supply, which risks should the agency be most concerned with?

Would you like to take a crack at that, Dr. Nightingale?

Dr. NIGHTINGALE. I suppose that was one reason why the committee suggested—it was a very controversial recomemndation—that categories of risk be established in order to set priorities. The FDA could start with risks that were irreversible or serious and frequent, or irreversible and that presented hazards to particular population groups who could not make their own decisions, such as children, or the unborn. Rather than responding on an ad hoc basis, depending on the publicity surrounding a particular issue, the FDA could deal first with substances judged to be of high risk.

The CHAIRMAN. All right.

Dr. NIGHTINGALE. It was really an attempt to set priorities, which the committee recognized as being an important concern.

The CHAIRMAN. Dr. Fisher, do you agree with that?

Mr. FISHER. Well, first I would point out that there are risks associated with almost every aspect of life, including walking across the street to get here, and the perception of what constitutes risk is highly variable amongst individuals.

Second, I think it is useful to keep in mind some perspective relative to risks associated with foods. Foods grown and marketed in the United States contribute to one of the most safe food supplies in the world in terms of morbidity and mortality of the population.

Currently, FDA and USDA have certain legislative mandates and mechanisms to address major problems associated with risks, and we have a general outline of the categorization of risks; that is, we can expect risks in the food supply to be associated with toxic and pathogenic microorganisms, environmental contaminants such as heavy metals, naturally occurring toxicants, pesticide residues, and then substances that are intentionally added to food.

With sufficient resources and flexibility, the agencies can address these risks. However, I think a point that has been mentioned before bears on this discussion, and that is, advances in our understanding of biological processes and our ability to discern toxicity by ever increasingly sensitive toxicological methods are bringing to our attention biological effects that heretofore we did not know existed. The interpretation of the significance of such risks to human health is an active area related to the legislation but also an active area of scientific endeavor.

In the final analysis, I guess I would say those effects that are shown to be irreversible in terms of permanent alteration of human health are clearly the most important. But finding out what they are and determining specifically what the risks from those might be requires rigorous investigation and critical analysis.

The CHAIRMAN. What guidance should the Congress give the FDA in setting a standard of safety, in your opinions?

Dr. NIGHTINGALE. Could you repeat the question, please?

The CHAIRMAN. What guidance should we as Members of Congress give to the FDA in setting a standard of guidance with regard to food safety?

Dr. Nightingale. Well, that is a difficult question. I wish Dr. Robbins were here because he would be better able to answer it than I, but I suppose that one kind of guidance that the Congress can give is that the Congress would reflect the public's views or perceptions of risks, that is, what the public views as important. The agency might have one set of priorities in mind, and the public might have another, and the Congress would be able to communicate what the public's concerns are, so that they can be dealt with by information dissemination, or other means, or regulations if justified.

One of the things that the committee took into consideration very seriously was the public's participation in decisionmaking on these matters, because if it is not done that way, there will be a reaction which is counterproductive. It should be a reflection of the public's perception.

The Chairman. Dr. Fisher.

Mr. Fisher. I don't think I could disagree with Dr. Nightingale. I am reflecting on some of the testimony of Dr. Kennedy earlier.

Clearly, the definition that is now in the Code of Federal Regulations has a long history of use and relates to reasonable certainty, which includes the concept of a value judgment about what represents reasonable and includes recognition of the phrase "not harmful," which does not mean zero risk but rather risks being determined to be or agreed to be negligible.

Should Congress provide guidance on a standard of safety in legislation? First, I would say that there should be some uniformity in the evaluation of safety of substances added to food. Second, consideration should perhaps be given to those types of safety factors that have been alluded to earlier in discussions—that of one in a million over a lifetime as a point from which discussion might start or the traditional hundred fold safety factor.

The difficulty is that such safety factors have exceptions, and, scientifically, they are very difficult to defend because biological systems are dynamic not static. On the other hand, I suspect, from a legislative and legal point of view, it is nice to have a point in time to hang your hat on.

I think Congress should consider seriously giving FDA some guidance with respect to safety, and I certainly would suggest starting with the definition that is in the code and some of the modifications that have been proposed by committees of the academy as well as other working groups.

Dr. Nightingale. Could I just add to what I said earlier?

The Chairman. Sure.

Dr. Nightingale. The role of the public in decisionmaking is really very important. But the decisions finally have to be made primarily on the basis of the best scientific information available, and the general public might not have that available in expressing their perceptions or opinions on risk. And so one very important role is public education for informed participation in these matters, and even holding hearings such as this serves a very important role toward information of the public on these matters.

There also needs to be support and study of how best to communicate scientific information and particularly information about risks on which the public makes decisions, and that is a field that is really in its infancy.

The CHAIRMAN. Now, Dr. Fisher, in your testimony, you state that the Delaney clause does not permit the exercise of judgment. Could you elaborate on what you mean by that?

Mr. FISHER. There are several points which perhaps are pertinent. First, the law as currently stated, as I think I indicated, makes no distinction amongst the several types of chemicals or physical agents involved in cancer induction.

Evolving knowledge of the carcinogenic process suggests that some substances may induce cancer while others may promote cancer, and still others may modify the carcinogenic response.

Induction of cancer is considered to be irreversible by many investigators while promotion and modification may be affected by biological mechanisms and, in this context, may be potentially reversible.

A second point is that there are considerable data that suggest that dosage, schedule, route of administration, as well as genetic capabilities of the animal, exert profound effects on the carcinogenic process. Interpretation of results of carcinogenicity studies in animals requires critical analysis of these factors in order to eliminate the possibility of confounding or the possibility of occurrence by chance and the possibility of bias.

And then, of course, the most important of all is the evaluation of those results with respect to extrapolation to man.

Third, studies of carcinogenicity do involve this matter of animal studies and their extrapolation to man, which is perhaps the most difficult issue.

And, finally, as currently written, the law does not provide for the consideration of the possibility or the extent of risk to human health when only animal data are available. Two circumstances need to be kept in mind: First with certain food additives or food ingredients, there is a long history of use, so there is some epidemiological data, sometimes strong, sometimes relatively sparse, that may be available. But for new food ingredients, there is very little epidemiological data available, and the flexibility to approach this difference is not present in the law as currently written. So I think we are suggesting that modification of the law to allow this flexibility in the interpretation of scientific data by knowledgeable scientists and responsible health administrators would provide a better basis for exercising scientific judgment.

The CHAIRMAN. Well, thank you.

I am going to submit a variety of questions to you for answering. We will keep the record open so any Senator can submit questions to any person who has testified here today.

[Material subsequently supplied for the record follows:]

Additional questions prepared by Senator Hatch enclosed in June 27, 1983 letter forwarded by Ronald F. Docksai, Staff Director, to Dr. Kenneth D. Fisher, LSRO.

1) With a limit on resources, but with a seemingly infinite number of risks in the food supply, which risks should the Agency be concerned with?

First, I would point out that there are risks associated with almost every aspect of life; that is, everything has its risks and the perception of what constitutes risk is highly variable among persons. Second, it may be helpful to keep food safety as an issue in some perspective relative to risks. Foods grown and marketed in the United States constitute one of the most safe food supplies in the world in terms of morbidity and mortality of the population.

Currently, FDA and USDA have legislative mandates and regulatory mechanisms to address major potential risks which are generally known to be associated with:

1) toxigenic and pathogenic microorganisms;
2) environmental contaminants, such as heavy metals;
3) naturally occurring toxicants, such as mycotoxins;
4) pesticide residues;
5) substances intentionally added to foods, that is, food additives.

With sufficient resources and flexibility, these agencies can address potential risks or problems as they arise. However, one additional point might be made. Advances in our understanding of biological processes in living systems and advances in analytical capabilities to discern toxicity are bringing to our attention biological effects that heretofore we did not know existed. The interpretation of the significance of such effects in regard to risks to human health is an expanding and active area of scientific endeavor. Finally, those effects that are shown to be irreversible in terms of permanent alteration of human health are clearly the most important; but finding and determining biological effects of this type requires rigorous investigation and evaluation of results.

2) What guidance should the Congress give the FDA in setting a standard of safety?

The concept that "safe" implies reasonable certainty that a substance is not harmful under intended conditions of use is, I believe, a brief statement of FDA's historical interpretation of safe. This definition is included in the Code but not in the Federal Food, Drug and Cosmetic Act. "Reasonable certainty" includes the concept of value judgments based on available evidence deemed credible by knowledgeable scientists and should also include recognition that "not harmful" means risks to human health are negligible rather than totally absent. Again, value judgment by informed experts is necessary.

As stated earlier, safe does not mean no risk or zero risk. Should Congress decide to provide a definition of "safe" in any modifications to current law, the language should reflect that scientific studies cannot establish absolute safety or a point at which there are no adverse biological effects.

In a related matter, the GRAS review was based on the premise that FDA has the burden of proof if a GRAS substance is to be declared unsafe. For new food additives, sufficient and credible evidence must be provided prior to commercial use -- that is, premarketing clearance. Should Congress provide guidance on a standard of safety in legislation, consideration should be given to the current dichotomy and to instituting uniformity in evaluation of the safety of substances added to foods.

Finally, FDA should have flexibility to call on outside experts when questions of interpretation of scientific data related to safety and risk arise. Safety -- in terms of a safety factor, are matters of judgment based on available information and its interpretation. Safety factors of 10 to 1000 fold in applying results of animal studies to man have been traditional. More recently, the concept of quantitative risk assessment has carried with it the idea of risk at 1 per 1,000,000 over a lifetime. All such estimates may err on the conservative side but how much they err is not fixed or predictable as yet. Thus, guidance requires flexibility to assess the magnitude of possible safety to man, particularly in cases where only animal data are available.

3) Do techniques exist which allow us to differentiate between risks that are very small and risks that are large?

Yes, but they continue to be improved and require critical evaluation in regard to extrapolating results to the human situation. For example, most short-term microbial tests and acute and chronic animal studies employ dose response protocols. That is, one dose at a level that does show toxicity, one dose at a level that shows no observable effect, and one or more doses in between. These data, together with data on metabolic pathways, are useful when they can be related to information on possible human exposures. Such data are more useful when various levels of exposure exhibit dose responses, the nature of adverse responses is clear, and occurrence of responses is found in more than one species.

Determination of risks to human health -- that is, risk assessment -- requires that toxic properties of a substance be identified, that they be evaluated in terms of the possibility that humans exposed to the substance at certain exposure levels may be adversely affected. If information is adequate and evaluation possible, an informed judgment on potential risks can be made.

4) Dr. Fisher, in your testimony you state that the Delaney Clause does not permit the exercise of judgment. Could you elaborate?

Several points may be pertinent:

a) As currently stated, the law makes no distinction among the types of chemicals or physical agents involved in cancer induction. Further, evolving knowledge of the carcinogenic process suggests some substances may be inducers, while others are promoters or modifiers. Induction of cancer is thought to be irreversible, while promotion and modification may be affected by biological mechanisms and, in this context, are potentially reversible.

b) Secondly, considerable data suggest that dosage, schedule, route of administration, as well as genetic capabilities exert profound effects on the carcinogenic process. Interpretation of the results of carcinogenicity studies requires critical analysis of protocols to eliminate the possibility of confounding, chance, or bias; and to evaluate the results in terms of extrapolation to man.

c) Most frequently, studies of possible carcinogenicity involve animal studies and their extrapolation to man. The extrapolation involves reasoned judgment which is currently not possible.

d) Further, as currently written the law does not provide for consideration of the possibility of, or extent of, human risk when only animal data are available.

Unrelated to these four points is the observation that from a biological and medical perspective, the Delaney Clause speaks to but one irreversible health effect, cancer. Modern scientific study suggests there are other irreversible effects -- teratogenicity and mutagenicity may be equally critical factors in regard to human health.

Modification of the law to allow for the necessary flexibility in the interpretation of scientific and medical data by knowledgeable scientists and responsible health authorities would provide a basis for exercise of scientific judgment.

5) What factors, such as dosage level or metabolism, affect the relevancy of animal studies to humans?

. Scientific advances now permit useful correlations of subtle indications of toxicity in animals with a number of variables. Animal models can be selected having certain characteristics which are similar to those of humans, such as the rate of absorption of the test substance, blood levels obtained, tissue distribution, manner of excretion, and, more importantly, the rate and pattern of metabolism. Yet there are always other controllable factors that do affect the outcome of experiments such as the sex, health, and age of the animal, imposed stress, nature of the artificial diet, size and frequency of dose, route of administration, temperature, season, and altitude. Despite critical attention to a host of variables, results with any given animal may not be entirely applicable to human conditions. For these reasons, experimental results with animal studies require careful analysis and interpretation by knowledgeable scientists.

Based upon the information available during the GRAS Review and its interpretation by the Select Committee, it appears that those animal data that would be most useful as predictors of human response are those data obtained with experimental animals or a combination of experimental animal models in which the pharmacodynamics and pharmacokinetics of the test substance are as close as possible to those known to occur in man. Such studies include administration of the substance orally in food and include levels that might be considered characteristic of human dietary habits. Results obtained under such conditions can be extrapolated more confidently to humans.

6) What kind of evidence should the FDA have before it takes regulatory action against a suspected carcinogen?

Not an easy question to answer briefly. Such evidence should show that there is significant risk to humans at levels of exposure to the substance as it is intended to be used. This, of course, begs the question as to what is significant risk to humans. The law does not now clearly speak to this issue as the FDA response would depend on whether the suspected carcinogen was already in use (as a food additive or as a GRAS substance), or if the substance was proposed for use. In most cases, evidence from human studies would be lacking or insufficient. In such cases, evaluation of carcinogenic risk would, of necessity, require careful evaluation of any available epidemiological data but more importantly, evaluation of positive or negative evidence from experimental animal and other studies. Further, reasoned judgment suggests these data and their evaluation should be considered in terms of risk to human health associated with the reputed carcinogen.

Finally, what might be considered adequate evidence currently might not be considered adequate in the light of evolving scientific knowledge in the future. I recognize my answer is not explicit, but I would reiterate the need for flexibility and for mechanisms that allow FDA to seek outside scientific evaluation prior to reaching regulatory decisions. I do not believe it would serve the best interests of maintaining high standards of food safety to specify in the law exactly what scientific evidence is required.

7) A frequent criticism of the current statute is the FDA's lack of authority to balance both the risks and benefits of a food additive. Because of certain practical considerations, full risk-benefit analysis has rarely been advocated. What kind of benefits might appropriately be considered and under what circumstances?

Benefit/risk assessment is useful in the evaluation of the safety of preventive and therapeutic agents because in such instances both benefits and risks are experienced by the same individual. Further, it is theoretically possible to express the benefits in terms of countermorbidity and the risk of the adverse side effects of a given therapeutic agent in terms of morbidity. For example, in the field of immunization against various illnesses, responsible medical experts have concluded that for the United States, tetanus immunization should be carried out because medical benefits outweigh medical risks whereas smallpox vaccination should not be performed routinely because the potential benefits from the prevention of a disease with a remote possibility of occurrence are less than the medical risks and possible costs associated with mass immunization programs.

A similar situation exists for food ingredients where a benefit to health from their use might be judged to outweigh a risk to health. Vitamins and other essential dietary ingredients fall into this category. A scientific evaluation panel can assess their benefit to the health of the consumer at a given exposure level and weigh the benefit against the risk of harm to the same individual. Health benefits to most individuals might be judged to outweigh risks in such cases, and those substances would be considered "safe" for human consumption even at levels having only a narrow margin of safety. Although there are potential risks from food fortification with iron, vitamin D, and vitamin A, the Select Committee believed such risks to be outweighed by the widespread public health benefits.

I believe it is important to restrict benefit/risk considerations to health benefits versus health risks if such authority is provided in any legislation.

8) During the past decade, FDA has used widely divergent ways of evaluating important and controversial food safety issues. On some occasions, it has handled these matters internally. On other occasions such as saccharin, it has requested that the matter be studied by the National Academy of Sciences. The GRAS list review was conducted by the Federation of American Societies for Experimental Biology. With regard to cyclamates, the expert

advice on the National Cancer Institute was relied upon. On certain substances such as red dye number 2, special consultants were employed, and on red dye number 40, a special working group was put together. What is the best way to handle peer review? Isn't it widely recognized that such use of outside expert committees has, over the years, enhanced the credibility of scientific decisions made by the FDA?

First, let me point out that over the past two decades the FDA has explored and used a number of ways of evaluating controversial issues. It is useful to note that during this time period, reliance on these processes have enhanced the scientific credibility of FDA and the public's acceptance of FDA's decision-making processes. The use of external groups, the openness of the processes, the opportunity for input from all segments of the public and industry have all contributed to resolution of issues of food safety and public health.

I am not sure FDA, or any agency for that matter, has developed the "best" way to handle peer review. While I am admittedly biased by our experience over the past 20 years at the Federation, I do firmly believe that scientific panels, independently constituted by organizations whose major purpose for existence is science per se, appear to be the most acceptable means for undertaking these activities and obtaining unbiased evaluations of scientific information that can be utilized to undergird subsequent regulatory decisions.

Kenneth D. Fisher, Ph.D.

7-13-87
Date

The **Chairman**. I just want to mention to you that we appreciate the effort you have put forth and the testimony that you have given here today. It has been very helpful to the committee.

I would like to announce that, as I understand it, we are going to ask that each of the witnesses who has testified today will remain in this room immediately following this hearing, so that the press can chat with you and ask specific questions of you. I think that would be very helpful.

With that, we will recess these hearings until tomorrow.

Thank you so much.

Mr. **Fisher**. Thank you.

The **Chairman**. The hearing is now recessed.

[Whereupon, at 12:14 p.m., the committee recessed, to reconvene the following day, Thursday, June 9, 1983.]

OVERSIGHT OF FOOD SAFETY, 1983

THURSDAY, JUNE 9, 1983

U.S. SENATE,
COMMITTEE ON LABOR AND HUMAN RESOURCES
Washington, D.C.

The committee met, pursuant to recess, at 10:30 a.m., in room SD-430, Dirksen Senate Office Building, Senator Charles E. Grassley presiding pro tempore.

Present: Senators Grassley and Hatch.

OPENING STATEMENT OF SENATOR GRASSLEY

Senator GRASSLEY [presiding pro tempore]. On behalf of the Senate Committee on Labor and Human Resources, and for Senator Hatch, who will be here very shortly, I would like to welcome each of you to the second of 3 days of food safety hearings.

Important ground was covered during yesterday's session when former FDA Commissioners Dr. Donald Kennedy and Dr. Jere Goyan presented testimony and answered questions on various components of the food safety laws. Their views and observations, based on their experience as FDA Commissioners, raised many important points about the act.

I was struck by the extent to which these gentlemen agreed on three points: The food safety laws have generally worked well to protect the American public; scientific knowledge has advanced greatly since the food safety laws were last revised in 1958, and these advances have made parts of the present laws outmoded; and, third, the Food and Drug Administration is hampered in its ability to utilize its best scientific judgment in evaluating and in determining policy for various substances.

We will all be interested today to see to what extent our other distinguished witnesses will agree or disagree, both generally and specifically, with Dr. Kennedy's and Dr. Goyan's views.

Following the Commissioners, we then had Dr. Kenneth Fisher from the Federation of American Societies for Experimental Biology and Dr. Elena Nightengale from the National Academy of Sciences testify, and they underscored many points outlined by the Commissioners. They, too, recognized the vast progress that has been made in science and technology over the last decade, and identified the effect of this progress on existing food law.

Today we look forward to gaining an understanding of the nuts and bolts of the scientific issues that were broadly addressed yesterday. Therefore, I would like to call for our first panel, people that we are honored to hear—three panels, in fact, who will address issues pertaining to food toxicology, carcinogenesis, and risk assessment.

Congress must acquire an understanding of these complex subjects of we are to effectively determine the need for a revision of food law. We welcome the benefit of the expertise of the panel members, and we thank them for being with us this morning.

We are going to commence today with a food toxicology panel consisting of Dr. Theodore LaBuza, Dr. Paul Newberne, and Dr. Bert La Du—Senator Hatch has now arrived—so I would ask if you would take over from here, Mr. Chairman.

OPENING STATEMENT OF SENATOR HATCH

The CHAIRMAN. Well, thank you, Senator Grassley. I really appreciate your starting this morning.

Let me please apologize to all of you. We have for the last year and a half tried to resolve the school prayer amendment in the Constitution Subcommittee, which I also chair, so we scheduled that this morning at 9 a.m.

It is no secret that there has been a lot of conflict, not really conflict but a lot of disagreement over what is the best school prayer amendment to come out with. I even had a call from President Reagan this morning as to what he feels is the best, so we put out what he feels is the best and one other which, frankly, we feel is the best. It took us until this time to get that resolved, so please forgive us for that.

Let me again thank Senator Grassley for being here. He has agreed to help me with these hearings because I have some conflicts this morning and I cannot stay for the hearings, and I am tremendously grateful to him. Of course, he comes with knowledge in this area, representing the great State of Iowa.

Let's commence with our food toxicology panel. Dr. LaBuza comes to us from the University of Minnesota, where he is professor of food technology in the Department of Food Science and Nutrition—if you would come to the table, please. Dr. Newberne is from MIT, where he is a professor of nutritional pathology. Dr. La Du is a professor of pharmacology at the University of Michigan Medical School. He worked with the National Academy of Sciences Committee and on the, SCOGS Committee, the Select Committee on GRAS Substances.

Gentlemen, we appreciate the time and the effort you have taken in preparing your testimonies. We have asked that you limit your comments to 10 minutes so that we will have time for questions. We look forward to reviewing your prepared statements as part of the printed hearing record.

We will just say at the beginning of this hearing, so that we won't have to keep repeating it, that all prepared statements will go into the record as if fully delivered before the committee, but we do appreciate summarization so that we can ask some questions.

Let's turn to you first, Dr. LaBuza.

STATEMENT OF THEODORE P. LABUZA M.D., PROFESSOR OF FOOD TECHNOLOGY, DEPARTMENT OF FOOD SCIENCE AND NUTRITION, UNIVERSITY OF MINNESOTA

Dr. LaBuza. Thank you. I am Dr. Ted LaBuza of the University of Minnesota. Thank you, Senator, for inviting me here.

What my background is and what I have been asked to speak of is the impact of the present laws on food technologies. I am not a toxicologist, so I am presenting a contrasting viewpoint for this panel. What I have prepared as an outline for you is an outline of the background papers I have written on the impact of historical development in new food technologies.

Basically, up until the late 1700's and early 1800's, the processing technologies that were utilized in the world were the same all over—fermentation, drying, cold storage, baking, salting, and sugaring of foods. There really was no science background in terms of developing new technologies or understanding these methods of preservation.

It was in the late 1700's and through the 1800's that we got new technologies such as canning, refrigeration, freezing, and the industrial drying that we see today. Unfortunately, if one looks at the history of these developments one finds that the major impact to develop these technologies was due to either one of two things: war, the need to preserve foods for military situations; and second factors such as the weather and population growth that caused famine, so we had to develop new technologies for preserving foods for a longer period of time than having the hand-to-mouth type of food systems that we had in the past.

Since about 1950 on through, till recently, what we saw was the impact of science and engineering in the food preservation field. It was in the early 1940's that universities around the United States, developed food technology and food science departments that encompassed the older commodity type departments—such as a dairy department or a department in grains—then new departments started putting together science to develop a better food system for this country rather than relying on the old artisan methods of processing.

What has happened in that interim is that there are a number of new technologies, developed both within universities and within the food industry, that have a great potential for improving our food supply. However, because of the present laws there have been certain specific hinderances to furthering these technologies and getting them to be used. I would like to just mention a couple of these and then talk about some of the problems we might have in the future.

One of them—which is a personal one that I had worked on, in fact while I was teaching at MIT—was the development of a new chemical additive, 1-3 butane diol, which could be used in certain food products to inhibit the growth of bacteria and harmful organisms. In fact, it was clinically tested at the University of Nebraska, but since the amount of chemical that would be needed was so small—if it were ever approved—the income from sales of it was such that it was not worthwhile for the two major companies working in this area to spend the time and money to go into the expensive drawn-out process of determining whether or not it was a carcinogen in long-term chronic toxicity tests.

In fact, if we had intact at that time the type of decision tree process that was developed by the Food Safety Council, and what Food and Drug is looking for in terms of risk/benefit decision points in testing, that compound would probably never have to be tested for carcinogenicity since it was already shown to be clinically safe and a metabolizable compound. Therefore, here is an example, if we had a better set of laws or regulations one could have allowed the use of that chemical because in fact it was already being used in clinical situations as medical food or drug, rather than as a food, and there was really no harm from it. However, the food law said that it would have to be tested as a food additive to prove absence of carcinogenicity.

Another interesting situation which impacts on us today is the whole question of irradiation of foods. In 1958, when the food additives law was put together, a process—food irradiation, in fact—was deemed to be a food additive, and because of that today we do not really have the utilization of irradiation as a process for very, very useful things, such as extending the shelf life of fresh produce, something that in fact is being done in many European countries.

Looking to the present and to the future, I see some very important changes that are needed if we are going to have a better food supply. One important area I think we see right now is what I call the tailored nutrition food area. I break that down into three important areas.

One is what I call the special dietary foods for weight reduction. The whole incident with saccharin, of course, is what started all these hearings. There are many substances currently being tested right now for replacement of sugars or replacement of fats for use in weight reduction—and weight reduction, by the way, is probably one of the most serious health considerations in this country, since we have probably over 50 million people with excess weight. With the very few substances we have that can be used to make foods palatable as well as low in calories, we have a real problem. Unless we can find better substitutes, we are still going to have these same problems in the future.

Without, again, a simpler system, a system of looking at the chemical compounds that might have a potential for use, without some type of decisionmaking process allowing a risk assessment of that, all these substances will have to go through the long, drawnout procedure chronic toxicity test with the controversy that we always have in carcinogenic testing. Therefore, I think a better approach to risk assessment would certainly help in that area.

The second area is what I call the medical foods, or those foods that people perceive not as a drug but rather as supplying some type of perceived medical need—foods that would eliminate cancer (the whole issue of additive that we are talking about), foods that would eliminate heart disease or foods to control hypertension or dental caries. There are known substances that, if we tested them, they probably would cause reduction in disease and they could be used in foods. However, the question again is the expense and the expensive and long, procedures which give us at the most some controversial data. Is that worth it, versus some other, more logical risk assessment procedure to alleviate the problem and come to a more logical decision.

Then, the last area which I think the present food law will have a certain impact on, is what I call the area of "mood foods," which has not really been in the press very much but I think it is a very important thing. We are finding out much new information today, with the new analytical procedures that are coming up for finding low levels of natural carcinogens, in food. We are also finding out that natural foods have in them substances that work at the brain level and at the central nervous system level to create certain types of moods. There is the possibility, in grapefruit for example, that there is the possibility of something present that actually helps change your appetite control at very, very low levels, to help in weight reduction.

Once we begin discovering these things, the question is, how are we going to regulate? Are these foods now going to become drugs, because if you use them it is going to affect your mood? How are we going to look at these foods in the future? I think, again, this whole thing has to be tied between the risk assessment and the new technology.

That bears to the last fact arena which I think is going to have a very, very large impact in the future, and for which present law right now will probably inhibit dramatically any important work in this area. This is the utilization of genetic engineering for changing the food supply to make it better.

I look at it in terms of three areas: One, genetic engineering in the area of plant genetics, to improve hardiness of plants, to improve the nutrition of plants, and to change the metabolic factors of the food to make it more palatable, tastier, whatever. These new foods, if regulated as a new food additives, will slow down work in that area because of the low pay back. We have to really carefully look at a risk assessment approach as to what is happening in those foods rather than treat each one as a new additive. Regulatory guidelines would be absolutely necessary.

The second is utilization of genetic engineering to produce useful commodities. A good example, that is being worked on in several universities, is producing milk protein from bacteria, rather than having the cows out in the field eating grass and then making milk, which of course is important to our industrial economy but is not very economical in terms of producing single proteins like casein. If we make this casein will it be a new food additive subject to the Delaney clause? Then, another area is the production of so-called natural flavors: why, instead of having to extract strawberry flavor from a fresh strawberry can we get it from a safe bacteria?

These are just examples of the new technologies that will come in the future. How we will look at them in terms of the regulation of them from a food and drug standpoint is going to be very critical. The Delaney clause, in terms of assuming a zero risk, will have an impact in saying that in fact many of these products of genetic engineers should not be allowed at the present unless they get the full bore of safety testing even though we are already using them. With that, I doubt very much that most companies would be willing to spend the dollars and effort in doing the research in these areas, which in fact would inhibit technology. That is what my concern is. If we don't have the laws written in such a way as to make it important to work in these areas, we will never see the work going on.

With that, I will end right here, since the time is limited, and I will answer any questions later or now.

The **Chairman**. Well, thank you, Dr. LaBuza.

Let's turn to Dr. Newberne.

You will have to excuse me. I am on the budget conference as well and it is in full bloom up there. I am going to have to go to that. I just once again want to express my gratitude to my colleague for helping me with these hearings.

These hearings are extremely important. It is the first time, really, since 1958 that we have held hearings on a matter that involves much greater technological advancement over these last 25 years than anybody thought possible.

We will turn to you now, Dr. Newberne.

STATEMENT OF PAUL M. NEWBERNE, M.D., PROFESSOR OF NUTRITIONAL PATHOLOGY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY

Mr. **Newberne**. Thank you, Senator Hatch, Senator Grassley, and the committee, for inviting me to come and present my views on this very important subject.

First I would like to point out as I am sure others have already, that the realities of safety evaluation are not often understood completely. That is, with the best intentions people sometimes tend to believe that safety can be absolute; it cannot be. Safety is a relative thing, and we have to remember that in our efforts to evaluate it.

We have shifted from a society that had a political problem in obtaining a sufficient amount of food and distributing it properly to maintain a well-nourished population, to one where we have an abundance of food today. As a result societal values have changed. There is a feeling for risk, but there is also a feeling for benefit. The benefit, we hope, will outweigh any of the risks.

Over the past 20 years there have been a lot of scientific advances in toxicology. The methodology used today to evaluate food safety is based on identifying a so-called no effect level, applying certain safety factors, and then setting permissible concentrations.

There are some problems, however, that have developed because of our advances in methodology and knowledge. Our analytical capabilities have improved immensely. Whereas we were originally measuring things in percentage of the diet, we have come to measuring chemicals parts per million, to parts per billion, the latter equivalent to a penny out of $10 million; now we are measuring in parts per trillion, which is like a 6-inch leap on a journey to the Sun.

Therefore, identifying effects on cells by modern methods has also permitted a deeper insight into what chemicals do. We now know how, through biochemical techniques and electron microscopy, to identify more subtle defects in cells produced by chemicals, but in fact we don't quite know how to interpret them.

Modern toxicology is attempting to identify alternate methods for determining safety. We have now the so-called short term tests, the Ames test, and others that utilize bacterial and mammalian cell systems, but I think we have to remember that a toxic effect requires several steps, as does a carcinogenic effect. One or more of these is undoubtedly crucial, and if we can identify that one crucial step adequately, perhaps we only need to deal with that in terms of safety evaluation. It doesn't tell us much about the science of toxicology necessarily, but it does tell us whether or not there is a step that can be eliminated and prevent the irreparable damage that may be done by a particular chemical.

Coming to the interpretation of results of safety evaluations, we are dealing with the most difficult of the questions that are raised. In order to try to interpret this, we are making a very broad assumption that our animal tests are in fact telling us that the animal is responding the same as man will respond. This, in fact, is not always the case.

Although the animal tests are not necessarily the best in the world, they are certainly the best that we have today outside of testing materials in man, which is the ultimate. We obviously cannot use people for experimental animals, but where it is appropriate—and I should point out my feelings on this—some of the food additives could be tested in human populations after we have had a look at some of the animal data. I don't feel however that that is quite the same as some of the chemicals that are truly dangerous.

Factors that influence animal data are quite important. We know in testing with animals that there is a decided difference in the age, sex, strain, and the species that one uses. We attempt to find which one is going to metabolize a chemical as closely as possible to the way that people do it. That really is the ultimate aim, and is not always achievable. Diets in animal studies are exceedingly important. We know a great deal about how diet influences the way an animal responds to a certain chemical or toxin.

Now just a word about the pathology of cancer; I can pass over that very quickly. We really don't know what cancer is. We know what it does, and it is one of the most dreaded of human diseases. We make every effort to try to prevent exposure to things that will cause it.

There are, in the pathologist's terminology, tumors that are either benign or malignant. It is quite difficult, in fact, to always be sure you are dealing with a benign tumor, one that is not going to spread and kill the host, or a malignant one, one which is going to kill the host unless it is removed in one way or another.

We are dealing with a difficult situation in this case with some of our test animals, particularly the mouse, where we have a problem with a liver that responds with proliferation to a large number of chemicals, many of which we know are not carcinogens, and to other conditions, dietary factors, surgical procedures—partial hepatectomies, for example. The mouse will develop liver tumors without treatment, if allowed to live out a normal lifespan.

In extrapolating animal data to man, I want to point out that we don't use one single animal test or short-term predictive test as evidence of safety or of risk. We try to use the entire toxicological package, and not make the decision based on any one single test. It is here that we need to be able to make a more subjective judgment. We use statistics in attempting to assess what we find in animals in terms of numbers, but in the final analysis it is really not statistical significance, it is the biological significance that really counts in safety evaluations.

In my view the Delaney clause has served a very useful purpose over the years, and it has taken care of a lot of the needs that were apparent 20 or more years ago. I feel personally more comfortable that it is in place than I would feel if it were not. However, I do believe that there could be some modifications that would permit the regulation of food chemicals to be based more on judgment and scientific data than on strictly structured and restrictive clauses.

Therefore, the crux of our area of expertise is to develop a potential that will improve our evaluation of human hazard. We do need to broaden the toxicological data base, develop and validate more short-term tests, so that we can use these in forecasting what may happen in human populations. These very things are indeed going on now in many of the laboratories around the country, and we have a national program that is devoted to this, the national toxicological program [NTP].

We are developing rapidly in the field of toxicology, and the information coming from such studies is now being used in risk-benefit analyses, where we are dealing with risk and benefit, hoping to be able to have more benefit than risk.

Thank you.

[The prepared statement of Dr. Newberne follows:]

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Food Science
Biochemical Engineering
Toxicology
Neural and Endocrine Regulation

June 2, 1983

The Honorable Senator Orrin G. Hatch
Chairman, The Senate Committee of Labor
and Human Resources
The United States Senate
Washington, DC 20510

Dear Senator Hatch:

I'm pleased to have the opportunity to present my views on the current status of food safety evaluation, our ability to identify toxic substances and phenomena associated with them and on the difficulties encountered in attempting to extrapolate animal data to man. A few headings will be used to keep this highly complex subject more manageable in view of time and space limitations.

A. Background

First, I should like to point out that there is no such thing as absolute safety and that there is risk in virtually all of our activities including our food habits and the foods we eat. The public has been misled into believing that we can have all the benefits of an abundant, tasty and nutritious food supply without any element of risk. This, of course, is an ideal goal, but unachievable. A more rational, scientifically sound aim is to provide an abundant, attractive, nutritious food supply with the greatest benefit and the lowest risk measured by every reasonable method (Stumpf, 1982). Modern western society values regarding food differ from those of populations of several centuries ago (Hobbes, 1651; Locke, 1690) and from those of many nonwestern countries. Their difficulty was and is how to acquire an adequate food supply and how to deliver it to those who need it, primarily a political problem. Today, we are dealing with politics of another order; political decisions reflect societal values as illustrated graphically by the proposals of FDA and USDA on saccharin, nitrite and acrylonitrile, among others. These are compounds with demonstrated toxicity but with great benefit to some or all members of society. There is great difficulty in banning them in the face of perceived or recognized benefits to the public.

It is my belief that the regulatory agencies and the food industry are doing a good job, in the face of serious difficulties and limitations, of providing us with a safe and nutritious food supply. Their efforts are sometimes impeded by laws such as the Delaney clause which, in effect, dictates that any substance that is associated with cancer of any type, in any species, induced under any set of circumstances, cannot be added to our food supply. This is in contrast to naturally-occurring substances such as aflatoxins (Strong, 1976; Newberne, 1974) and nitrosamines, two classes of potent natural carcinogenic chemicals, which are permitted in foods at specified limits (Food Chemical News, 1977). The decision to permit low levels of aflatoxin and to decline to act on nitrosamines is clearly a realistic response to a situation where scientific and political judgment act in concert to provide a rational decision, one that still provides reasonable safety to the public.

B. Scientific Advances in Our Ability to Detect and Identify Toxic Substances

When I began my career in the evaluation of nutrients and basic cancer research more than a quarter century ago we were fortunate to be able to measure some chemicals in hundreds of parts per million. Ten years later however, as a result of improved instrumentation and methodology we were able to detect substances in single digit parts per million. This was the case with the food-borne aflatoxins, first identified in 1965 in United States staple food products in our laboratory at M.I.T. (Newberne, 1965). These highly potent carcinogens had been identified in mold cultures at about the same time by Wogan and colleagues (Wogan, 1965) and chemically characterized by then highly sophisticated techniques also done at M.I.T. We could measure these contaminants only in parts per million at that time. We can now measure aflatoxin B_1 in fractions of a part per billion. One part per billion is equivalent to one penny out of $10,000,000.

Science is now capable, using modern instrumentation, of measuring chemicals in our environment and in foods at levels of one part per trillion, equivalent to a six-inch leap on a journey to the sun. The point here is that our ability to measure and identify substances has far outstripped our capacity to judge what the levels mean in terms of human exposure.

In addition to being able to measure substances in increasingly smaller amounts, we are now capable of identifying effects on cells and in biological systems, unknown even a decade ago. Toxic effects on cellular organelles can be identified by biochemical and electron microscopic techniques some of which can predict later untoward events. For example, if a chemical injures mitochondria, the energy source of the cell is compromised and it can no longer function at a normal level, if at all. When the endoplasmic reticulum is damaged, protein synthesis including vital enzymes is disrupted, a peril to life if permanent or irreversible. We are now measuring the products (adducts) of a union between chemicals and cellular macromolecules (DNA, RNA, protein) which may be significant to the development of cancer. Equally important however, is the cell's ability to repair the damage and rid the cell of potentially damaging adducts. Rapid repair of adducts may result in little if any permanent injury; slow repair may allow permanent accumulation of damaging agents, disruption of genetic material, and perhaps, irreversible changes including cancer.

C. The Nature of Modern Toxicology

Modern toxicology utilizes epidemiological as well as experimental animal evidence to determine whether or not a substance may cause an undesirable effect. Epidemiologic data are used to design experimental animal studies which can address specific questions impossible to study in humans. Well-defined protocols have been designed to produce data relative to the safety of a given substance. A modern protocol (Newberne, 1982) will include the following tests as minimum:

1) An LD_{50} test in rodents, a dose that kills 50% of the test group animals.
2) Metabolism of the chemical in an appropriate species. This includes the absorption, distribution, metabolism and excretion.
3) Teratologic studies.
4) Reproductive studies through three generations.
5) Short-term predictive tests. These include bacterial (Ames) tests, tests in yeast, in animal and human cultured cell lines, in vivo tests to determine effect on chromosomes.
6) 90-day study in rodents.
7) 6 months - 1 year study in dogs.
8) 2-year study in two species of rodents.

To this lengthy series of tests are added special studies designed to answer questions relative to a particular aspect of the compound.

The short-term predictive tests are useful as screening devices but can not be used as the sole basis for regulatory decisions because the interpretation of them is not established. For example, about 20% of compounds tested will give false positive or false negative results.

Studies of test compound metabolism are especially useful since they reveal what happens to a compound in mammalian systems, permitting some insight into how humans utilize and dispose of it and indicating appropriate test species. A majority of chemicals to which human populations are exposed require metabolic activation before they produce an effect. Such activation, and also deactivation are achieved through enzymes, often located in the liver. Since not all species activate chemicals to the same series of metabolites it is important to know, if possible, the metabolites produced from a given chemical or closely related chemicals by humans and choose an animal species showing similar metabolism. These studies, combined with histopathologic assessment of test animal tissues from chronic studies provide the most useful information about compound safety.

D. Interpretation of the Results of Safety Evaluation

Following the above listed series of studies and data gathering, a most important final stage is interpretation of the results. This is a most difficult task and reflects the tenuous nature of toxicological evaluation. We make sometimes broad assumptions in our attempts to extrapolate from experimental animal to man, an impossible achievement but one that must be addressed. A basic assumption is that humans respond to the chemical in a manner identical or similar to the test animal, an assumption that is often in error. Nevertheless, it is the best approach we have and the experimental animal studies are essential, despite arguments for alternative methodologies and test systems. While alternatives may provide important information we must eventually come back to a whole animal system with all its enzymatic hormonal, metabolic complexities if we are to approach the human situation. Bacterial and cell culture systems do not possess such systems.

D.1. The Influence of Diet in Toxicological Testing

There are numerous reports and publications relative to the influence of diet on the response of humans and animals to toxic and carcinogenic substances (NAS Report, Diet, Nutrition and Cancer, 1982). Much of the work on dietary effects in animals has been done in our laboratory, (Newberne et al, 1966; Rogers and Newberne, 1971 etc.). It is now clear that safety evaluation of food chemicals requires attention to animal diets. Deficiency of methyl groups in the diet alters remarkably the effective carcinogenicity and toxicity of many chemicals (Rogers and Newberne). It has been shown in numerous studies that such simple dietary alterations as increasing the protein or the fat content can result in quite different results in test animals (Gellatly, Newberne, Rogers).

D.2. The Pathology of Cancer

No other disease in human experience strikes such stark terror in the hearts and minds of individuals as the prospect of being affected with cancer. Cancer is viewed as irreversible and leading to a painful and protracted illness, terminating in death. This view is not, of course, entirely correct, and recent advances in detection, treatment and prevention of cancer should help to relieve some of these anxieties. However, the disease is a major cause of morbidity and mortality in the US and elsewhere, and all efforts possible should be made to decrease it.

In safety evaluation studies in animals, cancer can occur in any organ or tissue after exposure to a carcinogenic chemical, material, or injury. Some chemicals however induce an equivocal proliferative tissue response. The most troublesome example occurs in the mouse liver. It is important to distinguish between benign proliferation or tumors and malignant tumors induced by chemical exposure in assessing the potential human risk of similar exposure.

D.3. The Mouse in Safety Evaluation

Our government pathologists working in safety evaluation and carcinogenesis, have abandoned the concept and practice of separating benign and malignant tumors so well established in human and veterinary pathology. They are now considering most rodent tumors as malignant. All proliferative lesions in the mouse liver are assumed to be malignant even though there is good evidence to the contrary. Mouse liver tumors occur in an incidence of 5-100% in many strains used in safety evaluation even when untreated. Moreover, the tumors in mouse livers often do not result in the biological behavior associated with cancer. They do not: 1) usually shorten lifespan, 2) invade surrounding tissues and 3) metastasize and result in death of the host. Therefore, in my view, in most cases the mouse liver tumor is not a cancer and not a reliable indicator of exposure to a true carcinogen. Despite these sound pathologic principles, many decisions in regulatory agencies are made on the basis of mouse liver nodules alone and all other extensive negative data are ignored. This is clearly ignoring sound biological principles and the fact that diet, housing, handling, surgical procedures, chronic injury, viral infections and many other nonspecific factors and conditions can sharply increase liver tumor incidence.

A species that already has a high incidence of tumors and which can be modulated by many factors or conditions is obviously not a suitable model for testing to provide results extrapolated to humans. Positive results, particularly liver tumors, in mice suggest a need for further studies using other systems but should not in themselves be regarded as sufficient evidence to label a compound a carcinogen or to ban it from the human environment.

While the above statements will be accepted by most rational pathologists, we will all agree that diagnoses of animal tumors are not simple and easy and that agreement on rodent liver tumors is almost non-existent. For this reason, future legislation should clearly state that rodent liver proliferative lesions will not be used as the sole determinant for a regulatory decision.

E. Extrapolation of Animal Data to Man

Despite the above cautionary statements, particularly about the mouse, animal studies are essential to the continued evaluation of chemical safety. With the exception of two substances (arsenic and benzene) all of the approximately 30 chemicals which are known to be human carcinogens also produce tumors in one or more laboratory animal species. Epidemiologic data are useful but are as imprecise and difficult to interpret as animal data. Taken together, and with sound scientific judgment, both can be used to estimate human risk. Animal data should be considered in its totality; everything (the toxicology package) must be factored into a final determination and no single test should be considered adequate for a decision. Chance alone will produce a positive effect in about one out of twenty trials.

F. The Use of Statistics in Safety Evaluation

Statistical tests are useful to confirm what we already strongly suspect or actually know. They should not be used to draw out tenuous differences in response of sensitive tissues to chemical exposure. Statistics should never be used as a sole mechanism for determining if a substance is safe or not. Our greatest concern must reside in biological rather than statistical significance. In recent years safety evaluations have provided an ever increasing list of diagnoses of background pathological changes which are available for statistical comparison. This produces some obtuse interpretations and such practices should be discouraged.

G. Toxicology Testing and Public Policy

As noted above, while there are gaps in our knowledge regarding the meaning of results of some testing procedures, when taken as a whole, and without excessive reliance on any single test, our system is working well to protect the public. However, in my view the conservative position sometimes taken by regulatory agencies may be depriving the public of valuable substances. An informed public will provide congress with an indication of its will, witness the cases of nitrite and of saccharin. For these reasons it is my view that results of safety tests should be taken seriously but with rational consideration based on sound scientific judgment in setting public policy. For these most difficult cases, regulatory agencies should be guided by decisions of expert committees comprised of appropriately trained and experienced scientists and lay personnel.

H. The Delaney Dilemma

The Delaney amendment has served a useful purpose over the past two decades and I personally feel more comfortable with it in place than I would if it were abolished. Progress in analytical procedures, biological testing systems and experience in making judgmental decisions clearly indicate however that some flexibility is needed in the face of equivocal animal data, or even positive tests in some cases. Regulatory decisions should be made in a milieu where science, judgment, and public benefit can be intermixed to the benefit of all. There should be legislation which, while keeping Delaney principles in place, permits or stipulates that regulatory bodies make judgmental decisions outside the rigid edict the amendment is now perceived to require.

Sincerely,

Paul M Newberne

Paul M. Newberne,
Professor of
Nutritional Pathology

Senator **Grassley**. Thank you, Dr. Newberne. We will go to Dr. La Du before we have questions.

Proceed, please.

STATEMENT OF BERT N. LA DU, M.D., PROFESSOR OF PHARMACOLOGY, UNIVERSITY OF MICHIGAN MEDICAL SCHOOL

Mr. **La Du**. Thank you, Senator Grassley. I appreciate the privilege of presenting testimony before this important committee, and thank you very much for inviting me to do so. I am going to paraphrase my written statement to some degree because of the short time that we have, and will only elaborate on those parts that seem to be somewhat different than testimony you have heard earlier.

I would like to say that in general I believe that the public is reasonably well-protected from hazards and contaminants in food at present, but there are changes that certainly can be made to improve both the regulations and the deficiencies of knowledge that we have in carrying out that mandate.

One of the things that Dr. Newberne mentioned that I would like to elaborate on, is that during the last 10 years there has certainly been increased care in toxicological testing to study ranges of concentrations of the substances being tested, from very low to very high dosage, because this information is so important in estimating the safe level of exposure, and we find different dose-response relationships to occur in different species, so it is important to take into account those differences in extrapolating information from several species to man.

We find, for example, in some cases that the rate of metabolism and detoxification of agents is quite different from one species to another. It is quite uncommon, however, to find intrinsic differences in the different species in the response to chemicals at the cellular level, so this helps us understand some of these differences and interpret them.

The rest of my statement will deal primarily with suggested changes that will increase our ability to monitor for chemicals added to foods, and prevent toxicity in the next decade or so. First, some regulatory changes that I would recommend on the basis of my experience as a member of the GRAS Committee review panel over the last 10 years:

We feel that food-grade standards should be established for all chemicals added to foods. The particular specifications and the amount of detail could certainly vary from chemical to chemical. This would depend upon the nature of the compound, its source, the type of impurities that might be present, and the method of preparation or isolation of it. Nonetheless, all such chemicals added to food should have some specifications in their composition.

The second is that efficacy should be demonstrated for any compound added to foods. Any chemical deliberately added to foods should serve some useful purpose and produce some worthwhile effect, such as greater stability, an antioxidant effect, enhance the flavor, or the like. Every claimed effect should be supported by scientific data demonstrating the effectiveness of that compound in that particular respect.

The third point is that we should develop uniform standards for all compounds, including those with GRAS status. Some chemicals enjoy GRAS status even though we have very limited biological and toxicological information about them. Although there is no serious adverse information about them or even suspicion, it does seem we should expect uniform standards for all the chemicals added to foods.

It is not scientifically acceptable to conclude that just because a chemical has been added to foods for a number of years, that this proves that it is safe and harmless. We would like to see, ultimately, the elimination of the special status of GRAS (Generally Recognized As Safe) substances, and eventually have a single system for dealing with the safety evaluation of all chemicals added to foods.

The fourth recommendation is some modification of the Delaney clause. There will obviously be some difficulties enforcing a new law that represents a modification of the Delaney clause. Nevertheless, it is time to allow some flexibility in the law and recognize that there are circumstances under which the presence of tumors in animals does not necessarily mean that the chemical represents a significant risk of cancer to man, if consumed in the amounts and manner approved.

The next section deals with research activities needing congressional support during the next decade to support the mandate of the FDA. The first I would make is improvements in the FDA intramural research program.

The FDA has an obligation to conduct two kinds of research activities. The first is what we would call applied research, directly related to its regulatory functions, where they are supplying certain tests and analyses needed to support legislative regulatory responsibilities. The second is basic or fundamental research related to the long-term responsibilities in connection with advances in the science related to food technology and scientific developments related to safety of foods.

There is no doubt that important aspects of the applied research program in the FDA should be strengthened, but the most serious deficiency I see is an inadequate commitment and a lack of specific budgetary obligation to maintain a high quality, scientifically recognized basic research program within the FDA. What is there needs to be expanded and greatly expanded.

For health sciences we have the National Institutes of Health. For agriculture we have regional laboratories and other excellent research facilities, but we have no equivalent strength in basic research in the intramural program, which is in support of an obligation of the Federal Government that is just as important in its own way as health care and agriculture.

The FDA is responsible for allowing hundreds of chemicals being added to foods that we consume over our entire lifetime, and the stakes are very high. Considering the odds, it is perhaps surprising we don't hear more often of problems in the FDA. However, under the present circumstances the FDA resources seem to be largely consumed in dealing with the problems that arise from time to time, and there is little time and budget left to study the longer term issues.

Some people have suggested that the longer term issues and needs of the FDA could be met by targeted programs and grants from NIH, or research activities in the Department of Agriculture, but neither of these mechanisms seems to be working very well and I am pessimistic that this is the way to go in the future. Food processing companies and food producers are also not going to solve these general, long-term problems on their own.

I would like to plead for a strong basic science program in the FDA, related to both drugs and food chemicals, that would deal with a number of the basic issues we have encountered over and over again in our review of the GRAS Substances. In fact, unless this is done I don't see how the FDA will be able to carry out its full responsibilities of protecting the public in respect to drug safety and food safety, considering how extensively food products are being modified by chemical treatments and additions and the future prospects of this being done on even a greater scale.

A modern food safety policy requires a sophisticated, very wise input of scientific expert knowledge at every level of legal and regulatory action. I think this can be best achieved by having a strong intermural research component within the FDA administrative structure.

Now some of the areas that need particular development in the future. First, the development of short-term tests of toxicity. High priority needs to be given to support the development and validation of new, short-term biological tests like those now available for testing mutagenicity. Similar tests are needed for other acute and chronic toxic events. These include carcinogenicity, teratogenicity, special organ damage, and harm to special sense organs—the eyes, ears, and so forth—bone marrow, reproductive tissues, and other specialized tissues.

The cost of the time and effort required to carry out the standard types of chronic toxicity testing in animals has become extremely high, as I am sure you know. It will take time and attention by devoted scientists to reach these objectives through short-term tests, but I am confident that we will eventually be able to obtain more useful information about the biological properties of new compounds with new, short-term tests to be developed, than by the standard chronic exposure tests now required by the FDA of applicants for new drugs and food additive chemicals.

Development of these new short-term tests depends upon our expanding knowledge of the mechanisms by which chemicals produce tissue damage. Once the mechanism is clear, it is not very complicated to see whether a new chemical directly, or through its biotransformation in the body to metabolic products, is able to carry out such reactions. Of course, there will have to be adequate validation and confirmation of these new tests against the accepted standard tests. To speed up the comparison, however, we have a number of information sources that can be used so it can go relatively swiftly.

I believe that it is likely to be easier to interpret the short-term tests that have predictive value, than the standard chronic animal exposure tests now generally used. For example, if the type of toxicity is well defined, the question of whether the toxicity is produced by the chemical given or a metabolite of the chemical can be answered. If man does not convert the chemical to the same toxic metabolite, then the toxicity findings in the animals may have relatively little direct application to human safety.

Other kinds of tests need to be developed that represent extensions of the current standard acute and chronic toxicity testing in animals. We need tests for behavioral effects, hypersensitivity reactions of an allergic nature, disturbances of endocrine balance, and some nutritional effects such as interactions with trace metals and vitamins.

Again, there is a need to develop new tests to detect evidence of such effects that will have predictive value for human use without waiting for the wide use of the chemicals in the population to reveal such unexpected reactions. There are likely to be subpopulation groups in our whole population at special risk due to diseases, genetic traits, and other special conditions such as pregnancy that are not adequately covered in standard toxicology testing.

The last two points I would like to make are general ones. One is further and additional use of safety panels and committees. There has been a move during the last few years to decrease the number of scientific panels and review committees used by the FDA. My experience in the GRAS Committee convinces me that calling upon the scientific community has been a useful and practical means of obtaining the advice it needs. I hope this committee will encourage the exchange and use of such resources to the FDA.

The last point I would like to raise is the public information responsibility of the FDA, and further support that may be needed there. The public has been bombarded by news reports and magazine articles about the dangerous and serious health menace of so many drugs and chemicals that we are exposed to, that there is almost a defensive disbelief in the validity of any of these adverse claims and charges.

There is a need for the FDA to assume a visible, leading role in educating the public and putting in proper perspective the current information about food chemicals and their safety. The FDA should be able to present an objective evaluation of such risks and present the current status of these controversial issues in way that would inform the public and restore confidence in that agency as one that operates to protect the public interests as well as to see that useful new products reach the marketplace. Additional funding may be needed to fill that particular obligation.

Thank you.

[The prepared statement of Dr. La Du follows:]

Statement for the Senate Committee on Labor and Human Resources hearings on Federal Food Safety laws, June 9, 1983, by Dr. Bert N. La Du, Department of Pharmacology, The University of Michigan Medical School, Ann Arbor, Michigan 48109.

Where are we now in respect to identifying hazards to health in food ingredients? I believe that the public is reasonably well protected from hazards and contaminants in food. On the whole, the regulations, as currently enforced, cover nearly all of the known and foreseeable dangers in food manufacturing, processing, storage and preservation. This does not mean that the laws and the scientific information related to federal food safety responsibilities are perfect or without need of change; a number of improvements should be made in the regulations, and we must correct some serious deficiencies in our knowledge relative to food safety and to food sciences. These deficiencies in information also exist in a number of relevant scientific areas, such as toxicology and nutrition, that are so important in the evaluation of the health aspects of food ingredients-- whether these chemicals are added intentionally or enter the food indirectly, in the course of processing, storage and from packaging materials.

During the past 10 years, as a member of the Select Committee on GRAS Substances, I saw a number of developments in safety evaluation methods. For example, the Ames test for mutagenicity became a commonly accepted and used test; most scientists now consider it to be a valuable screening method for identifying potentially mutagenic chemicals. Technical methods, e.g., high pressure liquid chromatography and gas chromatography, have made it possible to detect and quantitate the large number of components in some natural products. As an example, over 40 individual substances have been identified and measured in a product called liquid smoke, a condensate of wood smoke that has been partially purified to remove carcinogenic polycyclic hydrocarbons and retain the main ingredients of smoke that gives the usual smoky taste when added to meat, cheese and other food products.

In addition, the quality of acute and chronic toxicity testing in animals has improved. The tests generally include a search for possible effects on reproduction, growth and development, and look for adverse effects on organs by special tests of organ functions, particularly liver or kidney functions. These changes have given increasing weight and meaning to conclusions that state that "no adverse effects were noted." Greater use has also been made of radioactive tracer compounds to observe the fate of new chemicals. Statistical methods have improved for calculating risk to man, and extrapolating animal test results to human risk.

Another area, not new within the last 10 years but one that has certainly advanced during that time, is the increasing care in toxicological testing to study a range of concentrations of the agent being evaluated and to examine the dose-response relationship, from very low to high doses. This information is essential for estimating what a safe level of exposure might be, and in comparing results of tests in different animal species. Different dose-response relationships occur among species quite often, but usually these are explained by differences in rate of metabolism and detoxification, rather than intrinsic differences in response to chemicals at the cellular level.

What changes will increase our ability to monitor for chemicals added to foods and prevent toxicity in the next 10 years?

1. Regulatory changes requiring new legislation or modification of existing legislation, based upon our experience on the SCOGS Committee.

A. Food-Grade standards for all chemicals added to foods. There should be food-grade specifications for all chemicals added to foods. The rigidity of the specifications and the amount of detail can vary from chemical to chemical, depending upon the nature of the compound, its source, the type of impurities, and method of preparation or isolation.

B. Efficacy should be demonstrated for any compound added to foods. Any chemical deliberately added to foods should serve some useful purpose and produce some worthwhile effect, such as greater stability, an antioxidant effect, enhance the flavor, or the like. Each and every claimed effect should be supported by scientific data demonstrating the effectiveness of the compound in that respect.

C. Uniform standards for all compounds with GRAS status. A number of chemicals enjoy GRAS status even though we have very limited biological and toxicological information about them. Although there is no serious adverse information or serious suspicion about them, it is reasonable to expect uniform standards for all of these chemicals added to foods. Furthermore, it is not scientifically acceptable to conclude that because a chemical has been added to foods for many years and appears to be without harm, it must be really safe and harmless. In fact, we would like to see the elimination of the special status of GRAS substances and eventually have a single system for the safety evaluation for all chemicals added to foods.

D. Modification of the Delaney clause. There will obviously be some difficulties enforcing a new law that represents some modification in the Delaney clause. Nevertheless, it is time to allow some flexibility in the law and recognize that there are circumstances under which the presence of tumors in animals does not really mean that the chemical represents a significant risk of cancer to man, if consumed in the amounts and manner approved.

2. Research activities needing Congressional support during the next decade.

A. Improvements in the FDA Intramural Research Program. The FDA has an obligation to conduct two types of research activities: 1, applied research, directly related to its regulatory functions, to supply certain tests and analyses needed to support its legal responsibilities; and 2, basic or fundamental research related to its long-term responsibilities in connection with the advances in the sciences related to food technology and scientific developments related to food safety. No doubt there are important aspects of the applied research work of the FDA that should be strengthened, but the most serious deficiency I see is an inadequate commitment and lack of a specific budgetary obligation to maintain a high quality, scientifically recognized basic research program in the FDA. For the health sciences, we have the National Institutes of Health; for agriculture, we have the Regional Laboratories and other research facilities, but we have no equivalent basic research intramural program in support of a federal obligation just as important in its own way as health care and agriculture. The FDA is responsible for allowing hundreds of chemicals being added to foods that we consume over our entire lifetime, and the stakes are very high. Considering the odds, it is surprising that we do not hear of problems at the FDA more frequently than we do. However, the FDA resources are largely consumed in dealing with the problems that arise, and there is little time and budget left to study the longer-term issues. Some people have suggested that many of the long-term research needs of the FDA could be met by targeted programs and grants from N.I.H., or by research activities at the Department of Agriculture, but neither mechanism has worked, and it is unlikely that either will work in the future. Food processing companies and food producers are also not going to solve the general, long-term problems on their own.

I would like to plead for a strong basic science program in the FDA, related to both drugs and food chemicals, that would deal with a number of the basic issues we encountered over and over again in our review of the GRAS compounds. In fact, unless this is done, I don't see how the FDA will be able to carry out its full responsibility of protecting the public in respect to food safety, considering how extensively food products are being modified by chemical treatments and additions, and the future prospects of this being done on an even greater scale.

B. Development of short-term tests for toxicity. High priority in research support should be given to the development and validation of new, short-term biological tests like those now available for testing mutagenicity properties of chemicals. Similar tests are needed for other acute and chronic toxic events, such as carcinogenicity, teratogenicity, specific organ damage, and harm to special sense organs (eyes, ears, etc.), bone marrow, reproductive tissues, and other specialized tissues. The cost and time required to carry out the standard type of chronic toxicity tests in animals have become extremely expensive, as I'm sure you all know. It will take some time and attention by devoted scientists to reach these objectives, but I'm confident that we will eventually be able to learn more useful information about the biological properties of new compounds with new, short-term tests to be developed, than by the standard chronic exposure tests now required by the FDA of applicants for new drugs and food additive chemicals. Development of these new short-term tests depends upon our expanding knowledge of the mechanisms by which chemicals produce tissue damage. Once this is clear, it is not very complicated to see whether a new chemical directly, or by its biotransformation in the body to metabolic products, is able to carry out such a reaction. Of course, there will have to be a period of validation and confirmation of all such new tests against the accepted, standard tests, but we also have the large file of conventional tests results to speed up the comparison with the new short-term tests. The latter have not only the advantage that they will be rapid and much less expensive, but they are designed to examine very specifically and quantitatively the particular mechanisms of organ toxicity. I believe they are likely to be easier to interpret and have more accurate predictive value than the usual type of chronic animal exposure tests now generally conducted. For example, the type of toxicity is likely to be well defined, and the question of whether the toxicity is produced by the chemical given or a metabolite of the chemical is likely to be answered. If man does not convert the chemical to the same identified toxic metabolite but metabolizes the chemical to other products, the toxicity finding in the animal test system has little direct application to human safety.

C. Additional new methods to evaluate other types of toxicity. The standard acute and chronic toxicity tests in animals are not necessarily adequate to detect a number of types of toxicities, such as behavioral effects, hypersensitivity reactions of an allergic nature, disturbances of endocrine balance, and some nutritional effects, such as interactions with trace metals or vitamins. Again, there is a need to develop new tests to detect evidence of such effects that will have predictive value for human use without waiting for the wide use of the chemical in the population to reveal unexpected reactions.

D. Use of Scientific Panels and Committees. There has been a move during the last few years to decrease the number of scientific panels and review committees used by the FDA. My experience on the SCOGS Committee convinces me that calling upon the scientific community has been a useful and practical means of obtaining the advice its needs. I hope that this Committee will encourage the exchange of information and the use of these resources to the FDA.

3. Public Information Responsibility of the FDA

The public has been bombarded by news reports and magazine articles about the dangerous and serious health menace of so many drugs and the chemicals we are exposed to that there is almost a defensive disbelief in the validity of any of these adverse claims and charges. There is a need for the FDA to assume a visible, leading role in educating the public, and putting in proper perspective the current information about food chemicals and their safety. The FDA should be able to present an objective evaluation of such risks and present the current status of these controversial issues in a way that would inform the public and restore confidence in that Agency as one operating to protect the public interests as well as see that useful new products reach the marketplace.

Senator **GRASSLEY**. Thanks to each of you. I have just a few questions.

Then also let me make a general announcement, not only for this panel but for the succeeding panels: Since other members of the committee cannot be here, we may submit questions to you in writing because of time, particularly concerning the fact that we got started late.

I think the questions I have to some extent are more to focus attention, because you obviously have addressed to some degree some of the things that I am going to be asking. From that standpoint, I would have to consider your testimony very thorough, and I want to compliment you for it.

Dr. LaBuza, you have discussed what directions advances in food technology have taken. What kinds of statutory flexibility do we need to insure that our food safety laws can accommodate these advances?

Mr. **LABUZA**. My basic feeling is that the whole area of allowing the Food and Drug Administration to have some form of risk assessment, in terms of looking at either processes or new food additives, or finding things presently in foods that may be carcinogens—the ability to put them in the proper perspective and to have a risk assessment procedure much like they have put together in the FDA's "red book" or the Food Safety Council's "decision tree" process where they can say, "Well, given a series of steps, if the compound passes these we don't have to go any further because our experience shows that there is no need to do any further testing on this."

I think this will allow a more rapid development and allow for a better direction in research within the food industry for looking at new processes, new techniques, that will have a benefit to the country as a whole.

Senator **GRASSLEY**. Each of you, I assume—and I know particularly Dr. Newberne has—dealt with the FDA and probably know very well its inner workings. I want to know then, considering that, the extent to which you feel that Congress ought to make some of these basic decisions or establish broad policy and leave great detail to the FDA. We discussed this a little bit yesterday with Dr. Kennedy and Dr. Goyen and they had strong views on it. Do you have anything that you want to submit on that point, Dr. LaBuza, as a followup to your statements, or any of the rest of you, in response to my question?

Mr. LABUZA. My feeling is, I think the Congress has to set a standard of some sort. What that standard is going to be will be very difficult. Saying that Food and Drug can do risk assessment is words. Since I presently teach a course in food law, I know the real difficult problem of translating law into actual practice. I think the wisdom of Congress is good and after going through these hearings I think you should be able to deliberate enough to come up with what you think is the proper method to change the Delaney clause.

I think having the absolute standard that you have right now, in terms of zero risk in the Delaney clause, is controversial, is unnecessary because the law does already require safety and is an issue that does not allow any kind of risk assessment. Therefore, the law should be put in such a way that would give Food and Drug the ability to do risk assessment. I think you have good scientists there at FDA, you have good regulators there, and they know what their job is, and you will always have some type of overview. I think that charge is about as simple as it can be, writing the law in such a way to allow for that flexibility and then letting the Food and Drug to come up with the specifics in terms of regulations, of how they would carry this out.

Senator GRASSLEY. Dr. Newberne.

Mr. NEWBERNE. Yes; I would tend to agree with what Ted has said. Further, it seems to me there needs to be more flexibility permitted than is now either perceived—I am not sure it is totally built into the Delaney—but at least it is perceived as very rigid, and that often either permits or directs decisions that do not really use subjective judgment based on scientific information. Therefore, I have a feeling that there could be some adjustment from Congress that would then permit the regulatory people to deal in a more realistic way.

Senator GRASSLEY. Dr. La Du.

Mr. LA DU. I agree with the two other speakers in their statements. It is important to have the responsibility in Congress, recognizing that new changes in the law will certainly increase the complexity of carrying out the mandate of Congress.

What I am a little concerned about is if new money is needed to support the various activities within the FDA, that that is built into the system so that we don't have an increased responsibility forced upon the FDA without the resources to really do that mandate well.

Senator GRASSLEY. Dr. Newberne, in the background part of your letter that you sent to Senator Hatch as a summary of testimony, you make statements I very definitely agree with:

> There is no such thing as absolute safety. There is risk. The public has been misled into believing that we can all have the benefits of an abundant, tasty, nutritious food supply without any element of risk.

Then, of course, you say that this goal is unachievable.

To what extent—as you just said, for Government agencies to be realistic in their approach—for instance in the FDA, would this generally be an attitude that you have, or is there an attitude that somehow we can have a risk-free society, FDA as an example? I ask you because you have had lots of contacts with them. Do they share your view here?

Mr. NEWBERNE. Well, I hesitate to speak for them but I feel they——

Senator GRASSLEY. Well, I am not asking you to speak for them. I am asking you to give me your judgment, as you have had many communications with them. Do they share your view, as you would perceive it?

Mr. NEWBERNE. As I perceive it, I think they do share my views that they need more flexibility.

Senator GRASSLEY. Fine. Dr. Newberne—and this would also be to the other witnesses as well—in 1958 a substance was generally classified as either a carcinogen or a noncarcinogen. I would ask again for a focus, even though you did touch on it, what we have learned since 1958 about the parameters which affect the relevancy of animal studies to humans.

Mr. NEWBERNE. My view is that animal studies do indeed have a relevance to people. Interpreting and trying to extrapolate is a very difficult matter, and I think we have to take the best evidence we have and weigh it in its entirety, hopefully coming from animal species that metabolize certain chemicals similar to man.

With that in view, I think we can accept data today that perhaps is a little less extensive than we are now using, so I think the extrapolation is where we run into problems. Toxicology is a science and an art. The science we can develop; the art comes largely from experience in dealing with these things and showing, yes, by past experience certain things do happen and others do not.

I think that fairly well expresses my view. The newer things that are coming up that later speakers will address will deal with things that can be done in humans, as predictive. I think there is where we are heading.

Senator GRASSLEY. Dr. LaBuza.

Dr. LABUZA. Not being a toxicologist, but having looked at a lot of the data, I think that probably one of the most critical issues—which extends what Dr. Newberne is saying—is this whole problem of extrapolation. In 1958 I don't think there were toxicology departments anywhere. It really has been a developing science, and the big problem that still exists today is in the risk assessment area in terms of selecting the mathematical models that one is going to use to extrapolate the data from animals to humans.

I think the past 10 years, a generation of data showing where models apply and where they don't apply, does lead us to the conclusion that yes, indeed we can take these "decision tree" processes and find the most proper route for testing and the most logical route for testing, and not have to go through the test procedure that was envisioned in 1958, which was not really very easily extrapolated to humans. Therefore, I think there has been a lot of development but I agree we need a lot more research in this area, as Dr. La Du was saying.

Senator **Grassley**. Dr. La Du.

Dr. **La Du**. I would like to reemphasize my statement about the need for new testing that gets into the mechanism by which these chemicals produce their toxic effects. If we really understand that, it makes the problem of the appropriate animal and the extrapolation of the biological events that occur in animals to man much easier. It is where we don't know what the compound does that we test it in a sense to find out how much can be tolerated and then hope that with the extrapolation we are giving a safety margin to man in the same way. That is a much more difficult area. The more we know about mechanisms, the easier it will be, and the short-term tests will certainly complement the standard acute and chronic toxicity testing in animals that has been done for many years.

Senator **Grassley**. I think the points that I wanted to bring out and elaborate on have been elaborated sufficiently. Therefore, I want to thank each of you. You are each authorities in your areas. We appreciate your contribution to this dialog, and probably will be looking to you for some direction as we get down to more specifics. Thank you all very much.

Our second panel at this time will speak to the science of carcinogenesis. We will first hear from Dr. DeVita, Director of the National Cancer Institute. Following Dr. DeVita will be Dr. Wogan, who is chairman of the Department of Nutrition and Science at MIT. Also at MIT, he is professor of food toxicology.

Please proceed, Dr. DeVita, if you please. If you weren't here when Senator Hatch made the announcement, we would insert all of your testimony in the record and would appreciate your summarization at 10 minutes.

STATEMENT OF VINCENT T. DEVITA, JR., M.D., DIRECTOR, NATIONAL CANCER INSTITUTE, DEPARTMENT OF HEALTH AND HUMAN SERVICES

Dr. **DeVita**. Thank you, Senator Grassley. It is a pleasure to be here to talk about this important and interesting subject. In my summary I will focus on recent research advances in chemical carcinogenesis as they relate to our ability to detect carcinogens, and discuss what we are learning about the role of diet and nutrition in the causation and prevention of cancer, as well as what steps the Cancer Institute is taking to use this information.

Cancer is a disease characterized by unrestricted growth of abnormal cells. At present we divide this into two distinct stages. The first stage is referred to as "initiation," and it occurs as a consequence of the exposure of DNA, the cell's hereditary material to materials which damage it. The second stage is called "promotion," and generally requires a longer exposure time than does the initiation stage.

Promoters do not generally cause cancer directly but they facilitate the cancer process. Understanding the mode of action of these promoters is an important goal of carcinogenesis research, because there is evidence that removal or interference with the action of tumor promoters may be the simplest and the fastest way of reducing cancer incidence.

When we evaluate the risk of exposure to food additives, to naturally occurring chemicals in food, or other chemicals, the first step, as you have heard, is to consider the qualitative evidence that a given material is likely to be a carcinogen in humans. There are three ways of approaching this: first, the long-term bioassays in rodents; then, the in vitro tests, the tests with bacteria and tissue cultures; and finally, epidemiologic studies of whole human populations.

Recently two major areas of advances in science have influenced our ability to detect carcinogens: the development of techniques to measure small amounts of compounds, and a field we call "biochemical epidemiology."

I do want to comment a moment on the animal tests because I think there is an important point here. Of the 30 chemicals for which there is evidence of an association with cancer in humans, all—with the possible exception of arsenic—are risk factors for cancer in laboratory animals. Thus, the rodent bioassay appears to be a good predictor qualitatively for agents that are risk factors for cancer in humans.

However, there always has been a problem in interpreting these data because the dose in animal bioassay studies is purposely exaggerated to compensate for the small size of the animal study systems. In order to anticipate effects at low levels, the dose-response relationship must be extrapolated into the low-dose region. This region may be far below the dose used in the laboratory studies. Extrapolation, as you have heard, involves the use of mathematical models, and we don't have a single mathematical model that is useful in all cases.

It should be noted that these tests are tests for initiators. Initiators that have promoting activity at the same time are called complete carcinogens. It is known from several experimental studies that some initiators at low doses do not initiate carcinogenesis without concomitant promotion, so that some chemicals that are known to be carcinogens at high doses may not be carcinogens at low doses.

Highly sensitive analytical techniques have been developed during the last decade. They allow the detection in food of both naturally occurring and synthetic chemicals which are either already identified as carcinogens or, because of their chemical structures, are strong candidates for carcinogens in the rodent bioassay. These advances allow us to detect carcinogens at the parts-per-billion level or lower, as compared to parts-per-million level a decade ago.

With such techniques, we will likely be able to identify some traces of carcinogens in our food and water that are not possible to remove and that may have been present in these foods as long as they have been available. They may be at levels that are unable, as I indicated, to initiate carcinogenesis.

This is an emerging area of study. In fact, the presence of natural carcinogens in foods has not been studied very well until the availability of the Ames bacterial assay and the improvement in the methodologic techniques already mentioned.

Many reports are appearing in the literature now reporting carcinogens in food at very low levels. To cite two examples, one, urethane, a human carcinogen, has been detected in many foods and beverages made from fermentation, albeit at parts per billion levels; and polycyclic hydrocarbons, a class of chemicals in which carcinogens were first identified; has been detected in food, although usually at levels below 1 part per billion.

Epidemiology, the study of whole human populations, has clearly demonstrated the importance of environmental, occupational, and lifestyle factors. It is now practical to integrate laboratory determinations into the more classic epidemiologic approaches. This field is generally referred to as biochemical epidemiology.

The primary goal of biochemical epidemiology is to identify either evidence of high exposure of target cells in humans to carcinogens, or increased susceptibility due to inherited or acquired host factors. I would like to give you one example: For example, scientists can now measure the presence and the extent of carcinogen-DNA adducts, that is, a chemical bound tightly to DNA at the levels of one adduct per million DNA base. That is a very small amount.

These methods are based on newly developed, ultrasensitive enzyme radioimmunoassays, and they can make this test serve as a dosimeter for an individual patient's exposure to a carcinogen. The potential of biochemical and molecular epidemiology is to predict the risk on an individual basis instead of at the population level, and prior to the onset of clinically evident cancer. It provides an exciting new opportunity.

Our present findings strongly suggest that natural dietary factors are related to about 35 percent of all cancers in this country, but many of these factors appear to be acting as promoters in the diet, not as the classic initiators. By manipulating these factors, we may be able to reduce the incidence in mortality from some of the common cancers. These factors fall into two general classes: macronutrients, such as fat and fiber; and micronutrients, represented by vitamins, minerals, and trace elements.

Just a few selected examples of some of the evidence for this: Our cancer maps that we developed some years ago showed that the incidence in mortality from colon cancer in the southern part of the United States is lower than in the northeast part of the United States, in spite of the fact that most of the population being assayed in the southern States migrated from the northern States. This happened within a decade, so it seems as if some factor in the diet reduced the incidence in mortality from that particular disease.

We know that when Japanese women migrate from Japan to Hawaii to the United States, that their incidence of breast cancer rises from the low Japanese level to the high U.S. level. That seems to be related to changes in the fat content of their diet.

We know that in Norway smokers have a lower incidence of lung cancer when they have a higher incidence of vitamin A as measured in their blood using a vitamin A index. Altogether, there have been about 20 questionnaire studies that suggest an inverse correlation in various types of cancer between vitamin A consumption and beta-carotene, its precursor.

Thus, there is a growing body of evidence that indicates that cancer can be inhibited by specific agents which may exist in the diet. Most probably, this occurs by inhibiting the promotion stage, the second stage of carcinogenesis. The National Cancer Institute is attempting to use these agents, added to the diet, to reduce cancer incidence. This application of the results of basic research is called chemoprevention, and I summarize several of the studies in my whole document.

In summary, Senator Grassley, carcinogens which damage DNA are mostly initiators of the cancer process, and are now measurable in the most minute quantities, although they may not work as complete carcinogens as they do in large doses. We soon may be able to relate tissue levels in humans to the risk of developing cancer in individual patients, and correlate these with animal data which will make the animal tests much more precise predictors of carcinogenesis. The obverse of this is that the diet content, probably acting through the promotion stage, is a risk factor in cancer. By manipulation of dietary factors we may be able to decrease the incidence and mortality from common cancers.

This concludes my summary, and I would be happy to answer some questions.

[The prepared statement of Dr. De Vita follows:]

STATEMENT

BY

VINCENT T. DEVITA, JR., M.D.

DIRECTOR, NATIONAL CANCER INSTITUTE

NATIONAL INSTITUTES OF HEALTH

Mr. Chairman and Members of the Committee:

I appreciate the opportunity to appear before you today to discuss the recent developments in the science of carcinogenesis, and the direction that this science is likely to take in the next decade. In particular, I will focus on recent research advances in chemical carcinogenesis and discuss in some detail what we are learning about the role of diet and nutrition in the prevention of cancer. Our knowledge of the process of experimental cancer induction and our ability to detect mutagens and carcinogens has increased at a remarkable rate during the past decade. This increased knowledge leads us to believe that the role of dietary and nutrient substances is one key to understanding carcinogenesis. In fact, we now believe that dietary factors are in some way related to about 35% of all cancers.

Cancer is a disease characterized by unrestricted proliferation of abnormal cells. Although the early cellular and molecular events related to cancer causation are not completely understood, the neoplastic process appears to progress through several stages of development and a variety of factors can act to initiate or promote its development at each stage. At present, scientists separate this process into two distinct stages. The first stage, "initiation", occurs as a consequence of exposure to chemicals that damage DNA, the cell's hereditary material. The second stage is called "promotion" and generally requires a longer exposure time than does the initiation stage. Initiators include chemicals, radiation and viruses. Nutritional, hormonal, environmental, and genetic factors can act as promoters. Promoters do not cause cancer directly; they facilitate the carcinogenic process.

In the animal host, one or more enzyme systems may be required to activate a chemical to its carcinogenic form; any minor modification in the chemical structure of an agent could lead to profound changes in its metabolic pathway. Current evidence indicates that one of the earliest events in the process of carcinogenesis involves a structural change in the DNA of a target cell--a point mutation or perhaps more generalized damage to DNA--prior to its transformation into a cancer cell. Significant interactions may also occur epigenetically in the cytoplasm or at the cell surface. Nevertheless, it is possible that the carcinogen-bound or damaged DNA can be repaired, and the failure or inability to repair this damage may be linked to a propensity to get cancer. The damage may result in increased expression of a gene or increased production of a gene product which in some way regulates or controls cell growth and differentiation and may be responsible for maintaining the transformed (malignant) state. Finally, there may be other factors required for transformation to malignancy. Thus tumor promoters, hormones and growth factors may enhance or accelerate the expression of neoplastic potential in the latent or initiated cell. Understanding the mode of action of these promoters is an important goal in carcinogenesis research, because there is evidence that removal or interference with the action of tumor promoters may be the simplest way of reducing cancer incidence.

In evaluating the risk of exposure to food additives, to naturally-occurring chemicals in foods, or to any other chemical, the first step is to consider the qualitative evidence that the material is likely to be a carcinogen in humans. The basis for this evaluation is the results of several studies: long-term tests in small animals, such as the rodent bioassay; techniques employing bacteria and cells in tissue culture plates (in vitro tests); and epidemiologic studies.

The Role of Animal Tests

Of the 30 chemicals for which there is evidence of an association with cancer in humans, all (with the possible exception of arsenic) are risk factors for cancer in laboratory animals. Thus the rodent bioassay appears to be a good qualitative predictor of agents that are risk factors for cancer in humans. In the 1970's the National Cancer Institute (NCI) pioneered a carcinogenesis testing program through which scientists established a standardized way to evaluate the carcinogenic activity of chemicals in mice and rats. Identification of a substance as a carcinogen in these bioassays depended on showing that the test substance causes an increase in the incidence of tumors or a shortening of the interval between exposure and the appearance of a cancer.

Additional confirmation of carcinogenicity is provided by positive results observed in more than one animal species, in more than one bioassay or in different laboratories, and the demonstration that the occurrence of tumors follows a dose-dependent relationship. In animal bioassay studies, factors considered include the increase in tumor incidence in the treated group compared to controls, the number of tumors diagnosed per animal, and the percentage of tumors at a given site which are malignant. Contemporary control tumor rates are compared with those in the chemically treated group.

The dosage in animal bioassay studies is purposely exaggerated to compensate for the necessarily small study size of animal test systems. In order to anticipate effects at low levels, based on what experiments revealed at higher dose levels, the dose-response relationship must be extrapolated into the low-dose region. This region may be orders of magnitude below the dose level used in laboratory studies. Extrapolation from these studies involves the use of various mathematical models, and no single model can be accepted universally at the present time. The development and selection of models will be increasingly influenced by an expansion of our knowledge of underlying biological mechanisms, such as the interaction of carcinogens or their metabolites with DNA. In addition, chemicals evaluated in the bioassay program in the future may be tested at more than two dose levels and information on the pharmacokinetics of the compound may be used to help select the dose levels at which it is tested - these issues are currently being reviewed by the National Toxicology Program, National Institute of Environmental Health Sciences (NIEHS), to which NCI's bioassay program was transferred in 1981. Additional information about carcinogenicity of a compound is also obtained through numerous other studies, such as cell transformation studies, studies on binding to DNA, various genotoxicity assays, and metabolism studies (including those in which metabolism in species in which the long-term animal tests were conducted are compared with metabolism in humans who have been exposed). Most recently, human epithelial cells and tissue explants also have been used to provide information on potentially carcinogenic chemicals. Epidemiologic studies provide important information about carcinogenic effects in humans because they associate human cancer incidence with exposure to particular chemicals, industrial processes or lifestyle factors.

New Analytic Techniques

Highly sensitive analytical techniques have been developed during the last decade that will allow for the detection in foods of both naturally occurring and synthetic chemicals which either already have been identified as carcinogens or are, because of their chemical structures, strong candidates for carcinogens in the rodent bioassay. These advances in analytical techniques make it possible to detect synthetic and naturally occurring carcinogens at the parts per billion level or lower, as compared to the parts per million level possible a decade ago. These analytical techniques include innovations and improvements in fluorescence measurements, high pressure liquid chromatography, column and gas chromatography and nuclear magnetic resonance and mass spectrometry. As an example, gas chromatography with a modified thermal energy detector can detect N-nitrosamines - potent carcinogens in fish, rodents and nonhuman primates - in foodstuffs at less than parts per billion concentrations. The chemical structure is confirmed by mass spectrometry. Further advances in the future may make it possible to detect these compounds at levels which are an order of magnitude lower than parts per billion; such advances are likely to involve the use of monoclonal antibodies, enzyme immunoassays and radioimmunoassays. With such techniques it is likely we will be able to identify some traces of carcinogens in our food and water that are not possible to remove and have been present as long as these foods have been available.

The presence of carcinogens or mutagens in foods was not studied extensively until the development of the Ames' method for the detection of mutagens and the adoption of the methodologic improvements in analytical chemistry noted above. Thus, today the number of scientific reports concerning mutagens and carcinogens that occur naturally or are man made and are detected in our food are increasing; this trend probably will continue as the methods used in analytical chemistry improve and become more sophisticated. For example, ethyl carbamate (also known as urethane), is carcinogenic in mice and nonhuman primates, and has now been detected in many foods and beverages made through fermentation, albeit at parts per billion levels. It has been postulated that a reaction between carbamyl phosphate and ethanol produces urethane.

Aflatoxin B_1, a carcinogen in fish, fowl, rodents and nonhuman primates, is a natural carcinogen produced by several strains of a fungus called

Aspergillus flavus. This compound also has been related to a high incidence of liver cancer in certain parts of Asia and Africa. Routine analytical techniques can detect aflatoxin B_1 at levels of 1 part per billion, but with newer, more sensitive techniques concentrations of 0.01 part per billion can be detected. In the United States, aflatoxin B_1 or other aflatoxins can contaminate peanut and corn crops. There is usually no aflatoxin detectable in peanut oil due to refinement and purification processes; similarly, aflatoxin levels are usually lower (or undetectable) in peanut butter, but occasionally as much as 3 parts per billion are present. In 1980 approximately 70% of the corn crop in some southern states was contaminated with aflatoxin, although the corn crops in the midwest were not contaminated to this extent. The actionable level by the Food and Drug Administration (FDA) for foods and feeds is 20 parts per billion.

The polycyclic aromatic hydrocarbons are the class of chemicals in which carcinogens were first identified. Most of the more potent carcinogens in this group have more than three benzene rings, hence the name polycyclic aromatic hydrocarbons. At least 15 different polycyclic aromatic hydrocarbons have been detected in food, and this list and the foods that contain them will surely increase as analytical methodology improves. For example, benzo(a)pyrene usually occurs at levels of 1 part per billion or lower in spinach, carrots, head lettuce, tea leaves, coffee, bread, rice and potatoes. Presumably, the major source of benzo(a)pyrene in plants is uptake from the soil as a result of burning, forest fires, volcanoes, industry and automobile exhausts, although definitive information is not available at this time. Benzo(a)pyrene also occurs in seafood and in smoked and barbecued meats.

Some plants containing carcinogens are actually promoted in nature books as good trail food, herbal remedies or teas. The bracken fern (*Pterildium aquilium*) often is eaten as a salad when in the "fiddlehead" or crozier stage, and any number of books on plants mention it as a wild food source. However, a component of this plant, which has yet to be identified, causes liver, bladder and intestinal tumors in rats. Gourmets, too, have habits that put them in contact with carcinogens. Components of tarragon vinegar, made from tarragon plants, and a delectable mushroom called the false morel both show weak carcinogenic activity in mice. But most people do not overindulge in tarragon vinegar or false morels, and the occasional use of these foods will probably not lead to cancer.

Biochemical Epidemiology

Scientific opportunities generally arise when two or more research areas converge and/or advances in methodology occur. Research in the laboratory recently has provided us with both critical information on mechanism(s) of carcinogenesis and new technological advancements including those in molecular biology. Epidemiology has clearly demonstrated the importance of environmental, occupational and lifestyle factors. It now is practical to integrate laboratory determinations into more classical epidemiological approaches to chronic disease. Thus the National Cancer Institute is placing great emphasis on a new field of research termed "biochemical or molecular epidemiology."

The primary goal of biochemical epidemiology is to identify individuals at high cancer risk by obtaining pathobiological evidence of (a) high exposure of target cells to carcinogens and/or (b) increased susceptibility due to inherited or acquired host factors. Included are efforts to incorporate already developed biochemical techniques into epidemiologic investigations and the further development and refinement of new experimental procedures into safe, accurate, reliable and informative adjuncts to human investigations.

Biochemical techniques currently available allow scientists to better characterize exposure to carcinogens, to identify intermediate points on the path to malignancy, to develop measures which halt or reverse this process, and to investigate the mechanisms of human carcinogenesis. Included in these investigations would be the following: (1) efforts to evaluate body burden of chemical carcinogens in studies of occupational and general environmental cancer risk factors; (2) sophisticated analyses of air, water, and biologic specimens for carcinogenic and mutagenic substances in conjunction with specific analytic studies; (3) investigation of the relationship between micronutrients and a variety of epithelial cancers; (4) determination of the relationship between macronutrients, including dietary fat and subsequent hormonal changes, to subsequent risk of breast, endometrial and perhaps colon cancer; (5) search for evidence of viral infection including viral segments or oncogenes in the DNA of individuals at high risk of cancer that may be associated with infectious agents or heritable states; and (6) evaluation of disturbances in immune function as they may relate to malignancies, particularly those of the hematopoietic system.

Advances in laboratory methods recently have been used in combination with analytical epidemiology to identify individuals at high cancer risk. These methods include: (1) techniques to assess specific host susceptibility factors, such as immunologic status, endocrine factors, efficiency of DNA repair, and susceptibility to cell transformation; (2) assays that detect carcinogens in human tissues, cells, and fluids; (3) cellular assays to measure pathobiological evidence of exposure to carcinogens; and (4) methods to measure early biochemical and molecular responses to carcinogens. For example, scientists can measure the presence and extent of carcinogen-DNA adduct formation in cells and explanted tissue from humans exposed to known or suspected carcinogens. This measurement is based on a newly-developed technique which uses ultrasensitive enzyme radioimmunoassay to measure carcinogen-DNA adducts. The covalent binding of the activated form of a carcinogen to DNA may be viewed as both a pathobiological dosimeter of environmental exposure to a carcinogen and as a predictor of an individual's metabolic balance between carcinogen activation and deactivation and his capacity for DNA repair. Ultrasensitive enzyme radioimmunoassays to measure carcinogen-DNA adducts are 100-fold more sensitive than radioimmunoassays and are now being used in pilot laboratory-epidemiology studies. A wide variation in the amount of this type of genotoxic damage has been found in high risk groups due to occupation (e.g., foundry workers and asphalt workers) or personal habits (e.g., tobacco smoking). Based on the data base from studies in experimental carcinogenesis, individuals with high levels of carcinogen-DNA adducts may be at increased cancer risk. The potential of biochemical and molecular epidemiology to predict cancer risk on an individual basis, instead of a population level, and prior to the onset of clinically evident cancer provides an exciting new opportunity in cancer research and cancer prevention.

Nutritional Factors and Cancer

Another significant and recent development in the science of carcinogenesis is the recognition that there may be an important relationship between nutritional status, general dietary patterns, specific foods, food groups and food additives and cancer. Certain diets and foods seem able to initiate carcinogenesis; others seem able to promote it; while still others seem able to reduce cancer risk. The mechanism of action can be through direct interaction with DNA, or indirect through alteration of the cell membrane and metabolic pathways or cell regulation, or even more indirect through modification of the endocrine or immune systems. Further research on diet and cancer, in which both epidemiology and laboratory science must cooperate, should yield insights into these mechanisms and the biology of carcinogenesis.

Thus far, data from epidemiologic and animal studies have not fully defined the roles of fat and fiber in the causation of cancer. For example, it is not completely understood how specific changes in the intake of fat and fiber might contribute to prevention of cancer. In addition to fat and fiber, other dietary factors under investigation to determine their influence in enhancing or inhibiting carcinogenesis include total caloric balance, vitamins and pro-vitamins (specifically A, C, and E), minerals (especially selenium and zinc), and naturally occurring compounds such as aflatoxin and other mutagens found in foods. In addition, there is increasing evidence that various methods used to cook foods produce compounds which are hydrocarbon derivatives or are derivatives of amino acids with highly mutagenic potential. The National Cancer Institute is currently assessing methods of food preparation and the resultant mutagens for their potential ability to cause cancer as well as factors in the diet that may prevent the development of cancer.

Laboratory studies indicate that retinoids, the set of molecules comprising vitamin A and its synthetic analogues, may prevent the development of some forms of cancer. One drawback to the widespread use of large doses of vitamin A and of retinoids always has been their toxic side effects. However, the National Cancer Institute has made progress recently in the development of new agents that are less toxic and can be more accurately directed to specific organ sites.

Other cancer inhibitors as identified by studies in tissue culture models or in animal studies are antioxidants (substances which retard oxidation, e.g., vitamins C and E), trace metals, protease inhibitors (compounds which inhibit proteolytic enzymes and may prevent formation of free radicals), indoles (constituents of cruciferous vegetables such as cabbage, cauliflower, and Brussels sprout), prostaglandin synthetase inhibitors (compounds that inhibit the formation of long-chain hydroxy fatty acids), and various nucleophiles (chemicals which serve as electron donors).

Examples of important findings related to diet and nutrition and other life-style factors are as follows:

- For a number of years, it has been noted that the incidence of certain cancers among the Utah population is lower than that of any other area of the United States. This was thought to be due primarily to differences in life style, since a large proportion of the population in Utah (approximately 70%) are members of the Mormon Church. The use of tobacco, alcohol, coffee and tea is proscribed by this religious group. Recent studies have compared cancer rates between the Mormon population and the total United States population. For cancers identified from earlier studies as related to cigarette smoking (i.e., lung, larynx, tongue, gum and mouth, pharynx, esophagus, pancreas, kidney and bladder) the incidence in Mormons is about 55% less than that in the United States population. In contrast, the incidence of these cancers among non-Mormons in Utah is only about 7% below that for the United States. The risk of cancer of the colon and rectum among the Mormon population is about 40% below the United States rate. Fat in the diet has been considered a possible risk factor for these cancers, but there is little evidence that the Mormon population consumes less fat than the general United States population. This population, however, eats more natural foods high in dietary fiber, a factor which is thought to be protective against colorectal cancer. The difference in alcohol consumption among the non-Mormon compared with the Mormon population is three-fold. The incidence of those cancers thought to be associated with alcohol consumption (cancers of the mouth, larynx and esophagus), is about 60% lower among the Mormon population than among the United States population; there is no decreased risk for these cancers among the non-Mormon population of Utah. Studies are underway to clarify the role of various dietary components, including micronutrients in this low-risk population.

- U.S. cancer maps prepared by NCI epidemiologists clearly have shown that colorectal cancer mortality rates for white men and women were lower in the South, by about 50%, than in the Northeast or North Central states. A close examination of the age-specific cancer mortality rates in those counties in Florida where Northerners move at retirement revealed that despite the large number of Northerners in these counties, mortality rates for colorectal cancer were as low as the rates in other Southern counties and did not seem to rise toward Northern rates at any age, not even at the older ages after retirement. A case-control study has been implemented to define precisely the characteristics of this reduction in risk and to quantify it. It was also of interest to see whether it might be due to the migrants being a self-selected subset of Northerners, since it is possible that only healthy Northerners choose to migrate. If this last hypothesis is not the explanation, a second study will be designed to identify the attributes of the Southern environment or lifestyle that are involved in reducing cancer risk--possibly increased consumption of fruits and vegetables or more vitamin A or C or the quality of the drinking water;

- Washington, D.C. is the U.S. metropolitan area with the highest rate of esophageal cancer for black males, the group in which esophageal cancer predominates. A case-control study revealed that poor nutrition and heavy alcohol consumption were the major risk factors. The risk due to poor nutrition was independent of the risk associated with alcohol. The least nourished third of the study population had about twice the risk of the most nourished third. When extremes of nutritional status were compared, the relative risk reached 13. There was no evidence for a specific vitamin deficiency. Instead, generally poor nutrition seemed to be able to increase the susceptibility of the esophagus in these urban black men;

- In contrast, a case-control study of the role of diet in producing the high rates of oral and pharyngeal cancer among white women in North Carolina suggested that fruit and vegetables were the food groups consistently lacking in the diet of the cases. Other basic food groups were not marginal among the cases, so generally poor nutrition did not seem to be the explanation. Both carotene and vitamin C intake are highly correlated with fruit and vegetable consumption. Although snuff dipping and smoking are the primary risk factors for oral and pharyngeal cancer among these Southern women, diet also seems to play a role;

- When Japanese women migrate to the U.S., their low rates of breast cancer rise toward American rates over a period of several generations. A case-control study of Oriental-American women living in Los Angeles, San Francisco, and Honolulu will attempt to identify during what period of the lifespan diet is operative in promoting breast cancer risk and to assess what aspects of Western diet might be involved;

- A case-control study of cervical cancer, now underway in five Comprehensive Cancer Centers across the U.S., will be the first to evaluate diet in a large number of patients with clearly invasive cervical cancer. Low intake of several micronutrients--vitamin A, carotene, folacin, vitamin C and vitamin E--has been hypothesized to increase the risk of cervical cancer or cancer in general. To complement the dietary interview, blood samples will be collected to measure serum micronutrient levels in the cases and controls directly;

- In Norway, smokers with a high index of vitamin A intake (calculated from dietary survey data) were shown to have a somewhat lower lung cancer risk than those consuming less vitamin A. Carrots, milk, and eggs were the main contributors to the vitamin A index. Confirmatory studies have been reported in the United States. Limitations of this type of study should, however, be noted. For example, it is possible that an index derived from vegetable intake may actually be a marker of something other than vitamin A. Shekelle and colleagues in Illinois suggest that the benefit may be related more to the dietary beta-carotene precursor than to vitamin A itself. Altogether about 20 questionnaire studies suggest an inverse association between vitamin A or beta-carotene and various types of human cancer. Two studies of retinol (vitamin A) levels in frozen sera found lower retinol levels for individuals who later developed cancer than for a comparable control group.

In summary, a growing body of basic and epidemiological evidence suggests that cancer can be inhibited by specific agents, probably by inhibiting the promotion stage. This chemoprevention of cancer is a new research area to ascertain if natural or synthetic agents can lower the incidence of cancer in humans. The National Cancer Institute is placing increased emphasis on basic research in chemoprevention intramurally and extramurally. Several intervention trials already have begun. They include a study of beta-carotene to be taken by physicians to prevent cancer; an investigation of a natural retinoid applied in a gel form to the cervix to see if progression from dysplasia to cervical cancer can be prevented; and the treatment with retinoids of patients with familial polyposis to see if their almost certain progression to colon cancer can be prevented. Additionally, several studies are being planned which aim at preventing new skin cancers in persons who have had previous skin cancers.

Dietary Guidelines

In closing, I would like to mention a major report which summarizes the scientific evidence linking diet and nutritional factors to cancer in humans. This report, entitled "Diet, Nutrition and Cancer" is a survey of the scientific literature conducted by an ad hoc committee of the National Research Council, which is a component of the National Academy of Sciences. The report is the result of a study commissioned by the NCI three years ago.

In their report, the Council said the evidence they reviewed suggested that cancers of most major sites are influenced by dietary patterns. They said also that additional studies are needed to quantify the contribution of diet to overall cancer risk and to determine what impact dietary modifications might have on cancer incidence. Based on their assesment of the scientific literature, the Council proposed some interim dietary guidelines. They suggested that Americans:

- Reduce the proportion of calories in the diet provided by fats.
- Include in the daily diet whole-grain cereals, fruits, and vegetables, especially those high in vitamin C and beta-carotene. These foods include citrus fruits, dark green and deep yellow vegetables, and members of the family cruciferae (such as cabbage, broccoli, cauliflower, and Brussels sprout).
- Minimize the consumption of salt-cured, salt-pickled, and smoked foods. These foods are associated with an increased incidence of cancers at certain sites, particulary the stomach and esophagus.
- Avoid excessive consumption of alcohol, particulary in combination with cigarette smoking. Such consumption has been associated with an increased risk of cancer of the upper gastrointestinal and respiratory tracts as well as with other adverse health effects.

The committee is now working on a second report that will make recommendations to the NCI on future efforts needed in the field of diet, nutrition, and cancer research.

This concludes my prepared statement on the research advances in chemical carcinogenesis and nutrition and the advances that may take place in the next five years. I would be pleased to answer questions at this time.

Senator **Grassley**. Would you wait until Dr. Wogan concludes his testimony?

Dr. **DeVita**. Certainly.

Senator **Grassley**. Would you proceed, please?

STATEMENT OF GERALD WOGAN, M.D., CHAIRMAN, DEPARTMENT OF NUTRITION AND FOOD SCIENCE, MASSACHUSETTS INSTITUTE OF TECHNOLOGY

Dr. **Wogan**. Thank you, sir.

In reviewing the progress in knowledge about the process of carcinogenesis, I have tried to condense what I feel are several aspects of the field which bear most directly on the question that is before this committee, that is, the possible modification of the law, particularly with respect to the Delaney clause as it relates to human risk assessment. I want to make, three major points, and these will in some ways reinforce and elaborate upon points that Dr. DeVita has already touched upon.

The first deals with the question of the knowledge about the nature of the carcinogenesis process itself, and here over the past 25 years there has been an enormous increase in understanding about the details of the process. It is now quite generally accepted that the process is divisible at least into two phases, the initiation stage and a progression stage(s), which clearly are different with respect to the underlying mechanisms and therefore in the way in which they can be dealt with.

The initiation phase is a very quick response which occurs rapidly after exposure to carcinogens. It is irreversible. It involves damage to the genetic apparatus of cells, which induces a heritable kind of change and which is then passed on from mother cell to daughter cell, leading eventually to tumor formation.

The progression phase, on the other hand, is a much longer process. This refers to the stages following initiation and continuing through the full development of recognizable tumors. This is a poorly understood process, one which undoubtedly has many stages within it. These are of indeterminate number but most importantly, in this context, the progression phase can be markedly affected by enhancing agents which do not in themselves otherwise induce tumors, the so-called tumor promoters.

This kind of understanding, it seems to me, provides a sound scientific rationale for the classification of carcinogens into two broad categories: Those that are initiating agents, and are referred to as genotoxic compounds; and those tumor inducors that are not initiating agents, i.e., the nongenotoxic agents or epigenetic carcinogens, as they are sometimes called.

In the context of the Delaney clause, it seems to me one of its most serious limitations is that it does not permit the regulatory agencies to take into account this differentiation which the science soundly supports. Promoting agents display threshold properties, dose-response characteristics in which there are levels of exposure that do not induce tumors under controlled conditions, and therefore which in principle ought to allow such substances to be dealt with differently than those agents which act through the initiation process. That is the first point.

The second point that I wanted to make is in a related area and has to do with the issue of potency of carcinogens. If we look at the entire literature dealing with carcinogens in animal systems that is available today—that is, all of those adequately controlled tests for induction of cancer by chemicals—roughly 300 compounds have been identified so far which everyone would agree are carcinogenic.

The way the Delaney clause views the subject is that substances are either carcinogenic or they are not carcinogenic. If however one looks at the details of those experiments, and particularly in respect to the kinds of levels that were administered to animals that were effective in inducing tumors, one finds effective doses that extend over a range of roughly a millionfold. That is, some substances are very powerful carcinogens; others are very weak carcinogens.

The Delaney clause, at least as it is currently interpreted and has been in the past, does not permit an accounting of the potency factor. This, again, in scientific terms seems not be to be a full use of the scientific data base that is available.

The final point that I would make has to do with the area of epidemiology. I think everyone agrees that the best information relevant to making decisions about human safety is information that is gained from studies in humans themselves, direct epidemiologic studies.

The great difficulty in epidemiology, particularly of chronic diseases such as cancer has been that such studies tend to be of very limited sensitivity in detecting carcinogenic insults because, among other things, the level of exposure often cannot be quantified with any degree of accuracy. There is a technology now developing which will permit using either chemical or cellular technologies to quantify exposures of individuals in the human population at ambient levels of chemicals, which would permit several undertakings to be done.

One would be to conduct parallel studies in human populations and in appropriate animal models, and to compare the dose-response relationships, the cancer outcomes, and so on in those two circumstances, and therefore greatly enhance the validity with which extrapolation can be done. Second, it should be possible to identify, using those technologies, high-risk groups which are the main groups of concern in relation to exposure, particularly to weakly carcinogenic materials.

Therefore, I think these three lines of evidence which have accumulated over the last 25 years are ones which bear quite directly on the question at hand. It seems to me that a change in the language of the Delaney clause which would permit adequate protection but introduce sufficient flexibility for the science to be taken into account would be a very worthwhile undertaking.

Senator **Grassley**. Thank you, Dr. Wogan.

One of the last questions I was going to ask, I will start out with first, because I think your second point just dealt with it when you discuss the weak and strong carcinogens. That is another way of saying that all carcinogens do not pose the same hazard. Right?

Dr. **Wogan**. Yes.

Senator **Grassley**. I was going to ask if they did.

Dr. DeVita, in your statement you give the example of vinegar as being a weak carcinogen in mice. You go on to say that the occasional use of such a substance is not harmful. Is it fair to infer from your example that potency and exposure are critical elements that must be considered in food safety decisions?

Dr. **DeVita**. I think so, Senator Grassley. We were referring to tarragon in tarragon vinegar which has a carcinogenic effect, and it is used in such small amounts generally that I think you can say that there is a relationship between dose and the risk of carcinogenesis.

This bears on a point I made before, that some chemicals at very low doses—even though at very high doses they may cause cancer—may not cause cancer at very low doses because they are not complete carcinogens. Therefore, there may be a threshold. If one wants to assume that you must have no risk, then one assumes there is no threshold and we just back-extrapolate to the very low dose.

My guess is, from what we know and what Dr. Wogan has talked about—the combination of initiators and promoters—that there may be some chemicals that at low doses require a promoter and without it, they will not cause cancer. Tarragon vinegar may be a good example of that.

Senator **Grassley**. Dr. Wogan, would you care to comment?

Dr. **Wogan**. Yes, I quite agree that while the term "threshold" has come to have unfortunate connotations, unnecessarily controversial, in fact in population studies—even when powerful carcinogenic stimuli are studied such as cigarette smoking or exposure to aflatoxin,—when such studies are properly done and the data are pooled there is, in both instances a clearly delineated dose-response relationship. Furthermore, there are levels of exposure below which there is not a detectible increase in risk of the forms of cancer that are involved. Therefore, this I think is quite consistent with the idea of minimal risk, if not a threshold effect.

Senator **Grassley**. Again starting with Dr. DeVita—but, Dr. Wogan, if you would care to comment—I asked the previous panel about the Delaney clause requiring a substance to be either classified as a carcinogen or a noncarcinogen, and I wanted your views on whether or not the distinction is always that black and white.

Dr. **DeVita**. No, I don't think so, Senator Grassley. I think that, again getting back to some of the issues we have already touched on, that there certainly is evidence in rodent systems—some studies, elegant studies, done by Dr. Roswell K. Boutwell at Wisconsin—that some carcinogens can be reduced to a dose that will not cause cancer in the absence of rather prolonged exposure to a promoter. Therefore, you may not have that black-and-white distinction.

Senator **Grassley**. I guess you have commented on it already. Do you want to say something more?

Dr. **Wogan**. Yes, if I could just add one or two other points. I think in part the origin of the idea that substances either were or were not carcinogens, as a black-or-white situation, arose historically as a result of the way in which the testing was done, in particular the whole concept of the so-called maximum tolerated dose which was used simply to determine whether one could obtain any indication of carcinogenic effect.

These were not intended to provide data appropriate for risk assessment, and indeed such experiments did not. Unfortunately, much of the literature that is available today from all sources is produced by that kind of testing procedure, and will therefore have limited usefulness for the risk assessment process.

Senator GRASSLEY. Let's carry some of the areas we have discussed to their implications for the regulatory policy decisions that we have to create the environment for with our legislation. As it might relate to the facts—like, for instance, you stated that different substances, like the initiators and the promoters, play different roles in the carcinogenic process—what is that implication as we try to regulate?

Dr. DEVITA. Well, we don't have very many good tests for promoters, so at the moment they are not identified as carcinogens, and yet substances in our diet, for example fat and fiber, may serve as either promoters or antipromoters. Manipulation of these in our diet may be very important, even though they are not regulated.

However, we have initiators that are tightly regulated that may not be able to work without a promoter. Therefore, I think—as I heard the other speakers this morning and Dr. Wogan comment—that in a way we are all in favor of flexibility in making judgments based on the best available scientific data—data, which now strongly favor this two-stage version of cancer and therefore has to be taken into account.

Senator GRASSLEY. Do you have anything you want to say on that, Dr. Wogan?

Dr. WOGAN. I would simply add that because of the fact that most of the short-term assays that we have, the presumptive tests for carcinogenicity, are in fact based on their ability to detect initiating agents. Because these have been widely applied, we know that there are a large number of initiating agents in the environment, including some that are produced in the ordinary cooking of foods, for example.

Therefore, while we know a great deal about the number and character of initiating agents, we know very much less about promoting agents, for as Dr. DeVita said, there are really no good assays at the moment for promoting activity that are related to the food question specifically. As a consequence, I think the tendency is then to regard—and probably appropriately so—initiating agents as more hazardous than promoting agents.

Senator GRASSLEY. I have no further questions but you may receive some in writing. Therefore, thank you all very much for your contributions to the discussion.

Dr. DEVITA. Thank you, Senator.

Senator GRASSLEY. Our third and final panel for today will address risk assessment. On this panel are Dr. Joseph Rodericks, Dr. Gilbert Omenn, and Dr. Reuel Stallones.

Dr. Roderick is a principal with Environ Corp., the Washington, D.C. consulting firm specializing in risk-related exposure to toxic substances. He was with the FDA for 15 years, during which time he served as deputy associate commissioner and as chairman on the Interagency Work Group on risk assessment.

Dr. Omenn is dean of the School of Public Health and Community Medicine at the University of Washington in Seattle, and under the Carter administration he served in senior positions at the Office of Science and Technology Policy. He was specifically concerned with Federal decisionmaking for public health risk at that time.

I hope, Dr. Stallones, that I pronounced your name right. He is presently serving as the dean of the School of Public Health at the University of Texas. He was chairman of the Committee on Assessment of Risks to Public Health; that was a study recently released by the National Academy of Sciences.

I think I will have you proceed in that order. Dr. Rodericks.

STATEMENT OF JOSEPH V. RODERICKS, PH. D., PRINCIPAL, ENVIRON CORP., WASHINGTON, D.C.

Dr. RODERICKS. Thank you, Senator Grassley. I submitted written testimony which is a bit lengthy. I am going to just recite some key points from that testimony for you.

The major points I would like to make are the following: First, that the assessment of human health risks associated with environmental agents is inherently an inexact science. In most cases, those of us who assess risks for environmental agents must rely on indirect evidence. We must make inferences about possible human health risks from information collected under conditions quite different from those to which humans are exposed. Nonetheless, methods of evaluation have been developed that permit identification of the range of exposure conditions under which the risk of harm to humans is likely to be extremely low, if not zero.

For substances that cause adverse health effects other than cancer, the assessment methodology usually involves the use of a large safety factor to insure that the maximum level of human exposure to a substance is only a small fraction of that required to produce toxicity. I stress that this widely used approach, which does not incorporate an explicit quantification of risk, does not insure the complete absence of risk—we have no way to insure that—but it almost certainly insures that risks are so low they are of no public health consequence.

Risk assessment methods are also available to evaluate data concerning carcinogens and to predict the magnitude of risk that they may pose. At some stages of this assessment process the methods of evaluation are different in character from those we use for noncarcinogens. I want to spend my remaining time talking about the methods used for carcinogenic risk assessment and why I believe they can be relied upon for safety decisionmaking.

I note now, and will discuss again at the close of my remarks, that the application of this risk assessment methodology yields only a view of the risk. Decisions on whether and to what extent any such predicted risks need to be further reduced are beyond the scope of risk assessment, but of course are the center of the debate on the degree of safety we should seek for food constituents.

Those who make safety decisions must have reason to believe that the risk assessment methods used are reliable in the sense that they discriminate among the risks posed by different substances and, when there is scientific uncertainty, as there almost always is, that they do not understate the risk posed by a substance.

If we are discusssing assessment of carcinogenic risks, I want to make one more point: The types of risks predicted by these assessment methods are distinct from the risks calculated on the basis of actual historical data concerning the relationship between certain activities—let's say, driving a car—and certain adverse outcomes—let's say, deaths from automobile accidents. The latter type of risk can be rather accurately calculated from historical data by actuarial statisticians, most of whom are employed by insurance companies.

The risks I shall be talking about here are those we predict might occur, on the basis of indirect evidence, usually from studies in animals, and are not based on the compilation of actuarial data on the actual incidence of disease or death. For these reasons, the predicted risks, which may sometimes be expressed numerically, should not be compared to risks calculated on the basis of actuarial data.

Therefore, having made that distinction, let me proceed to a brief discussion of the carcinogenic risk assessment process. I mentioned earlier that the safety assessment scheme used for noncarcinogens has not been considered appropriate for carcinogens. It has been assumed for some time that all toxic agents except carcinogens display what is called a threshold, a level of exposure that must be exceeded before toxicity of any kind is expected.

The difficulty we face in dealing with threshold agents is defining where that threshold might be in the human population when we have only animal data. Our method has been to incorporate safety factors to take that uncertainty into account but, as I said, there still remains a residue of uncertainty about the risk that might remain. We can be sure it is really quite low and of no public health consequence, but there is a residue of uncertainty.

Now many experts have maintained for some time that carcinogens produce their biological effects in ways that are fundamentally different from the ways other agents cause toxicity. The biological mechanisms by which carcinogens act are said to insure that any finite exposure, no matter how small, is likely to increase the risk—that is, the probability—of cancer development.

This does not mean that any exposure to a carcinogen will cause cancer to occur. It only implies, at the worst, an increased probability of cancer development. Therefore, it is in that context that, when we hear the phrase, "No exposure to a carcinogen can be considered safe," it must be viewed.

There are two attributes of carcinogens I would like to note. First, not all levels of exposure to a carcinogen are equally risky. Like other toxic agents, carcinogens obey the law of dose response. As exposure increases, so does the probability of cancer development; likewise, as exposure decreases risk decreases, and will at some finite exposure level become so, so small that most reasonable people would conclude that no public health benefit would be achieved by further reductions in risk. I make this statement while still accepting the assumption that carcinogens do not display thresholds, which may in many cases—as you have just heard—may be incorrect.

The other piece of important knowledge about carcinogens is that different carcinogens pose quite different risks at the same exposure level—that is, they differ in what is commonly called potencyk—and further, the magnitude of human exposure varies considerably from one carcinogen to another. The development of risk assessment methods has been based on the notion that these basic facts have to be taken into account if we are to distinguish important from unimportant risks.

The conduct of a risk assessment begins with the difficult task of review of information from animal tests as well as epidemiology data. At this stage of the analysis the assessor is not examining the ultimate question of the magnitude of risk humans might experience; rather, the assessor is only judging the strength of the evidence that a substance is likely to be a human carcinogen. There is great variation from one substance to another in the answer to that question. This determination only sets the stage for further analysis.

The next stages of risk assessment include analysis of information on underlying biological processes, or mechanisms as they have been called, and how they might affect the magnitude of risk; on the relationship between the level of carcinogen exposure and resulting risk; and characterization of the nature of this relationship in the range of actual human exposure. This information, coupled with data on the actual extent of human exposure, yields an estimate of risk.

This broad outline of the risk assessment process has hidden the fact I mentioned earlier, that to complete an assessment the risk assessor must make certain inferences and assumptions that, while biologically plausible, have not been subjected to empirical verification. As risk assessment is now practiced, the gaps in knowledge and information are filled by the insertion of assumptions that are designed to avoid understating the degree of human risk.

The cumulative effect of these assumptions is that in most cases, current methods of risk assessment not only distinguish among different risks but usually overstate the magnitude of human risk, although we cannot quantify the degree to which risk is ordinarily overstated. However, given this fact, it would seem to follow that the range of carcinogen exposures predicted under these methods to pose very low risks can be reliably assumed actually to pose very low risks.

The question of how low the risk is forced to go is, of course, not answered by the risk assessment itself. Those who must make such policy decisions must understand the results of a risk assessment. It is, therefore, necessary that risk assessors make quite explicit all of the assumptions and uncertainties that went into the assessment. Armed with such information, the policymaker can then analyze the likely public health consequences of a given action to determine whether the risk reduction is appropriate and how cautious this should be, given the extent of caution that has already been introduced into the risk assessment.

I will stop my remarks there. I have a recently prepared extended discussion of this same subject, Senator, that I would like to submit for the record if that is appropriate.

Senator **Grassley**. Yes, it is appropriate.

Dr. **Rodericks**. Thank you.

[The prepared statement of Dr. Rodericks follows:]

Testimony of
Joseph V. Rodricks, Ph.D.
ENVIRON Corp.
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Mr. Chairman and Members of the Committee:

I am Joseph V. Rodricks, a Principal of Environ Corporation, a scientific consulting firm. I am pleased to have this opportunity, along with my colleagues Dr. Omenn and Dr. Stallones, to participate in this discussion of risk assessment, and to contribute to the Committee's consideration of the broader scientific and policy issues associated with our Federal food safety laws.

For more than a decade, I have been involved in assessing the possible health effects of substances to which people may be exposed through food and the general environment. I worked for thirteen years in FDA's Bureau of Foods and for two years as the Agency's Deputy Associate Commissioner for Health Affairs. It is from this experience, and from that gained over the past three years by performing risk assessments for government agencies and for a variety of private clients, that the observations I make today are derived.

The major points I would like to make can be summarized briefly. First, the assessment of human health risks associated with environmental agents is, and always has been, an inexact science. This is true not only for carcinogens but for substances that produce a wide variety of other types of adverse health effects. In most cases, risk assessors must rely on indirect evidence -- that is, they must make inferences about the possible human health risks substances may pose under the conditions of exposure experienced by people from experimental and other types of information collected under different sets of conditions. Notwithstanding this inherent limitation in the science, methods of data evaluation have been developed that permit identification of the range of exposure conditions under which the risk of harm to humans is likely to be extremely low or even zero, and the range under which the risk may have a significant adverse impact upon the public health. For substances that can cause adverse health effects other than cancer (and all substances can be made to produce some form of toxicity under some conditions of exposure), the risk assessment methodology involves introduction of a large "safety factor" to ensure that the maximum level of human exposure to a substance is only a small fraction of the amount minimally needed to produce toxicity in experimental animals. This methodology, which has been in use for several decades, has gained wide acceptance in the international public health community. I must stress that this approach does not ensure the absence of health risk -- no approach could do that -- but it almost certainly ensures that risks are so low that they are of no public health consequence.

Risk assessment methods are also available to evaluate data concerning carcinogens, and to predict the magnitude of risk they may pose (or, more appropriately, the upper limit on this risk) under conditions of human exposure. These methods of evaluation are somewhat different in character from those used for non-carcinogens, and I shall spend my remaining time describing the nature of the carcinogenic risk assessment process, and why I believe it can be relied upon for safety decision-making. I emphasize that the application of this risk assessment methodology yields only a view of the upper limit on risk under given conditions of exposure; decisions on whether and to what extent any such predicted risk needs to be further reduced are beyond the scope of risk assessment, but, of course, are at the center of the debate on the degree of safety we should seek for food constituents. Those who make safety decisions must, of course, have reason to believe that the risk assessment methods used are reliable in the sense that they discriminate among the risks posed by different substances and that they do not understate the risk posed by a given substance. The methods now used to assess carcinogens and other types of substances meet these criteria of reliability.

Risk is the probability of harm. When we have available historical data on the relationship between certain activities and the occurrence of certain adverse events (e.g., the relationship between driving an automobile and deaths from automobile accidents), risk can be described with a relatively high degree of accuracy. Such actuarial risks, as they are called, take numerical values between zero (no risk) and one (100% probability of an adverse outcome). Within certain limitations, the risk of exposure to environmental agents may sometimes be similarly described by application of the methods of epidemiological science, the strengths and weaknesses of which others have already described. But in most cases it is not possible to collect the information necessary to make accurate risk calculations similar to those we can make for the risk of dying in an automobile accident. Of course, epidemiology studies are of no value at all when we have to decide whether a new substance can be safely introduced into food or other parts of the environment.

The risks due to environmental agents that we predict from indirect evidence -- usually controlled studies in experimental animals -- are quite different from those calculated from actuarial data. Current methods of risk assessment for such agents can not be claimed to yield accurate numerical measures of risk. These methods are designed to place an upper limit on the risk (i.e., the risk that will almost certainly not be exceeded and which will likely exceed the true risk), and also incorporate consideration of biological information that may not be readily expressed in numerical terms but which nevertheless influences the magnitude of risk. For these reasons, the risks I shall be describing should not be compared to those that are calculated on the basis of actuarial data. Having made this distinction, I shall now turn to a discussion of carcinogenic risk assessment.

I mentioned earlier that the safety assessment scheme used for non-carcinogens -- which is based on incorporation of a large safety margin -- has not been considered appropriate for carcinogens. It has been assumed for some time that all toxic agents, except carcinogens, display what is called a threshold -- a level of exposure that must be exceeded before toxicity is expected. The only difficulty we face in dealing with threshold agents is deciding where the threshold is for the large and biologically diverse human population when we have only experimental data. And, as I have pointed out, the methods we now use to identify the human threshold are limited and can not provide us complete assurance that we have done so. They only ensure that the risk at the predicted "human threshhold" is likely to be very low and of no public health consequence.

Many experts in chemical carcinogenesis have maintained for some time that such substances produce their biological effects in ways that are fundamentally different from the ways other agents cause toxicity. The biological mechanisms by which carcinogens act (which are by no means demonstrated in every case -- they are simply assumed on the basis of general theory) are said to ensure that any finite exposure, no matter how small, is likely to increase the risk of cancer development in an exposed population (this is simply the probability that cancer will develop). This does not mean that any exposure to a carcinogen will cause cancer to occur; it only implies an increased probability of cancer development. It is in this context that the commonly heard expression "no exposure to a carcinogen can be considered safe," must be viewed.

The methods now used to measure carcinogenic risks experimentally have been described by others, so I shall not review them. But there are two important aspects of our current knowledge about the attributes of carcinogens that I would like to note. First, not all levels of exposure to a carcinogen are equally risky. Like other toxic agents, carcinogens obey the law of dose-response -- as exposure increases, so does risk. It is also true that as exposure decreases, risk decreases and will, at some finite exposure level, become so small that most reasonable people would conclude that no public health benefit would be achieved by further reductions in exposure. I make this statement while still accepting the assumption that carcinogens do not display thresholds.

The second piece of knowledge about carcinogens that bears importantly upon safety decision-making is that different carcinogens pose quite different risks at the same exposure level. This fact is by now well-documented and is not in serious dispute. Moreover, human exposure to different carcinogens also varies widely. It is thus important that we make distinctions in the way we treat different carcinogens so that we do not neglect important risks and give undue attention to negligible risks.

The development during the last decade of methods for assessing carcinogenic risk was strongly influenced by the recognition of these attributes, and the need to take them into account.

The conduct of a risk assessment begins with the accumulation and critical review of information from animal tests as well as any available epidemiological data. For some substances this type of information may be substantial, but for others very few data will be available. The risk assessor's analysis consists of weighing the entire body of data and making a judgment about the strength of the evidence supporting the conclusion that a substance is or is not likely to be a human carcinogen. At this stage of the analysis, the assessor is not examining the critical and ultimate question of the likely magnitude of risk humans might experience under their actual conditions of exposure; the assessor is only determining whether humans are likely to respond biologically in the same way that experimental animals have responded to their exposures. This determination only sets the stage for further analysis.

The next stage of assessment concerns information about the underlying biological processes that led to the observed production of excess tumor incidence. Knowledge of underlying biological mechanisms can shed considerable light on the question of human risk, and analysis of information on such mechanisms is playing an increasingly important role in risk assessment. We must admit, however, that the types of data needed to gain knowledge about underlying chemical and biological processes are not now routinely collected, so that most current risk assessments can not incorporate such considerations. As you have heard from other witnesses, however, it is certain that this type of information will increase in importance in the future, and the tools of the risk assessor will thereby be strengthened.

The final stages of risk assessment include analysis of the relationship between the level of carcinogen exposure and resulting risk, and characterization of the nature of this relationship in the range of human exposures. This information, coupled with data on the actual extent of human exposure, and any available information on expected quantitative differences between humans and test animals, yields an estimate of the risk.

This broad outline of the risk assessment process has hidden the fact that I mentioned at the outset -- that to complete an assessment the risk assessor must make certain inferences and assumptions that, while biologically plausible, have not been subject to empirical verification. As risk assessment is now practiced, such gaps in knowledge and information (whether, for example, they concern the meaning for humans of data obtained in mice, the actual magnitude of human exposure, or the quantitative relationship between exposure and response at low levels of exposure) are filled by the insertion of assumptions that are designed to avoid understating human risk. The cumulative effect of these assumptions is that, in most cases, current methods of risk assessment will overstate the magnitude of human risk, sometimes substantially. Given this fact, it would seem to follow that the range of carcinogen exposures predicted under these methods to pose very low risks can be reliably assumed actually to pose very low risks.

The uncertainties associated with risk assessment, cannot, of course, be ignored. There is much additional research that should be done and further confirmation of the accuracy of the results of risk assessments is most desirable. Nevertheless, risk assessments are an essential and reliable aid in scientific regulatory decision-making, for without them, the decision-maker has no basis to differentiate between the potential health effects of various substances. The absence of complete certainty is no reason to opt for ignorance, and to make decisions that do not incorporate information on the health consequences of epidemiological episodes.

It is important to recognize that all methods currently in use and reasonably foreseeable to make the type of scientific decisions that we have been discussing contain an element of uncertainty. This is true for non-carcinogenic effects as well as carcinogenic ones. It is for this reason that it is critical that risk assessors make explicit all of the assumptions underlying their analysis so that the safety decision-maker understands the uncertainties in the predicted risk and its likely relation to the actual risk.

Deciding when the level of risk from a substance is of public health significance and when the risks, if any, are negligible from a public health standpoint, is not a part of risk assessment but involves a distinct analytical process that has a strong public policy component. The basic policy question is whether further reduction of a risk will provide a significant degree of public health protection. Under some statutes, this decision process must be further influenced by consideration of offsetting social and economic factors, but it can also be made based on consideration of public health benefits alone. FDA and other health protection agencies concerned with managing risks from chemical exposures have had to use these methods of analysis to establish acceptable levels of intake for carcinogens for a variety of classes of food constituents and other environmental agents, and I see no reason why the methods could not be universally applied. I believe, however, that agencies should take care not only to make explicit the analytic process used to assess risk and the uncertainties that accompany the assessment, but should also provide an explicit analysis of the decision process that led to a conclusion that a risk was significant or insignificant. I also suggest that the latter analysis should not be based on an *a priori* choice of a numerical value of risk that is said to divide significant from insignificant risks in all cases. A well conducted risk assessment contains a great deal of non-quantitative information that may be used to evaluate the relationship of the predicted numerical value of risk to the likely actual value (which can not now be predicted). Analysis of the public health consequences of a given predicted risk should incorporate consideration of the non-quantitative features of the risk assessment, and the extent to which the predicted risk is likely to overestimate the true risk.

I close my remarks by noting that too little attention has been paid to the basic reason risk assessment -- whether it concerns carcinogens or other types of toxic agents -- cannot be made more accurate than it now is. Uncertainties are high because fundamental knowledge is lacking. Research directed toward filling gaps in knowledge has not been especially well-supported. We spend a great deal of money testing chemicals for toxicity, which is clearly important, but we do not have anything like a comparable research effort devoted to furthering our understanding of the meaning of these toxicity test results for human health. I do not suggest that we should stop using the results of toxicity tests in deciding whether and to what extent chemical substances should be controlled; indeed, our current methods of safety evaluation seem to have served us well. But I do suggest that there should be closer attention paid to the fundamental reasons for the scientific uncertainties associated with risk assessment, and that any contemplated change in food safety laws should incorporate consideration of explicit provisions for research to fill fundamental gaps in knowledge.

(NOTE: In the interest of economy, a report entitled "Application of Risk Assessment to Food Safety Decision-Making," which is scheduled for publication in the September 1983 edition of Regulatory Toxicology & Pharmacology (vol 3, no. 3), was retained in the files of the committee where it may be researched upon request.)

DR. RODERICKS

ADDITIONAL QUESTIONS PREPARED BY SENATOR HATCH

1) During the hearings, reference was made to the risk of one in one million per lifetime (1×10^{-6}). Please explain what this means.

2) It is frequently said that quantitative risk assessment almost certainly overstates the actual risk because of the conservative assumptions used. Please describe these assumptions and why they are conservative.

Note: No reply to questions had been receive by press time.

Senator GRASSLEY. Thank you.
Dr. Omenn.

STATEMENT OF GILBERT S. OMENN, M.D., DEAN, SCHOOL OF PUBLIC HEALTH AND COMMUNITY MEDICINE, UNIVERSITY OF WASHINGTON

Mr. OMENN. Thank you, Senator Grassley. It is a pleasure to appear. I, too, have more extensive material for the record.

Senator GRASSLEY. OK. That will be included.

Mr. OMENN. The term "risk assessment," according to the National Research Council panel report and many other studies, means the characterization of the potential adverse health effects from exposures of people to specific environmental hazards.

Thus, risk assessments include descriptions of observable adverse health effects in various kinds of studies; extrapolations from those results to predict the types and estimate the probability of health effects in humans under given conditions of exposure; judgments about the number of persons exposed at various concentrations at various times and about the characteristics of those persons who are exposed; and finally, analyses of the existence, nature, and magnitude of the public health problems associated with such exposures, including explicit recognition of uncertainties inherent in the process of inferring risk. Risks must be characterized both qualitatively and quantitatively.

Risk assessment can begin only after data have been obtained from laboratory, clinical, and field research on health effects and exposures, combined with empirical and theoretical studies of methods for extrapolation. Risk assessment ordinarily should precede or be completed before the regulatory agencies, manufacturers, or consumers evaluate their risk management options and make decisions on regulation and production or use of particular substances.

Briefly, there are three major advantages of doing risk assessment, specifically in the area of food safety. First, risk assessment provides a framework for explicit analysis of the data on a particular substance. Both negative and positive results in various assays, full descriptions of a variety of effects—not just carcinogenic effects—and detailed information about possible mechanisms of action can be reviewed critically.

Second, risk assessment highlights the importance of dose and the whole issue of exposure, kinds of exposure, and the susceptibility of various subgroups in the population.

Third, risk assessment helps to differentiate what Johnny Carson would call the "biggies" from marginal or negligible hazards. Those responsible for assuring safety through their risk management decisions need such informative and intelligible characterizations of risk as inputs for decisions about safety.

There are three kinds of limitations that I believe should be emphasized: First, risk assessment cannot provide new results when research results are lacking or conflicting. Risk assessment provides a critical framework for interpreting results, and often identifies gaps in available data. Nevertheless, risk managers often must make decisions based upon the available evidence. It is not fair to blame the messenger when the evidence is limited or poor.

Second, characterization of risk at low-dose exposures requires extrapolation from observable effects in animals or highly exposed workers. We are forced to make models of the dose-response curve down to very low doses. Too often in doing the characterization of risk we are dealing with a "black box" situation comprising measured exposures, observed effects, and models of extrapolation. We do have high hopes that more detailed study of specific compounds for their mechanisms of action in producing cancers or birth defects or other damage will refine this extrapolation process, but we must not fool ourselves by thinking that such extrapolation will become unnecessary.

Finally, the linear dose-response extrapolation model widely utilized and widely accepted has the inevitable consequence that there will be some probability of risk at all doses of exposure greater than zero. For years we ignored this problem by assuming that if a substance were below any detectable level, the risk could be considered functionally equivalent to zero exposure. Stunning advances in analytical chemistry have given us powers of detection so enhanced that this convenient and pragmatic approach does not work. The FDA has been grappling for several years with policies and regulations about this problem of sensitivity of detection, and you have heard other people testify about that.

A corollary fiction is the "no-effect threshold" approach which Dr. Rodricks just described. For many health effects, just as in engineering bridges, it is assumed that a margin of safety can be introduced that reduces risk essentially to zero. In fact, at a conference just a month ago involving American and German experts about risk assessment, both for safety and health effects, safety engineers indicated that they are hostile to discussions about low-probability events. They rely on good principles of design and construction, and expect others to be satisfied that the results assure safety even though there surely may be residual risks.

The FDA uses this concept extensively in determining whether action levels are exceeded in various cases of food contaminants, I think quite appropriately. For carcinogenic food additives, as you know, however, this approach is not permitted by law.

It is my view that the estimation and characterization of risks should be the task of the scientists and risk assessors, but that the conclusions of adequate safety or insignificant risk must be drawn by policy officials, manufacturers, and consumers responsible for those risk management decisions—hopefully guided by the statutes and other actions of the Congress.

I know, Senator Grassley, through conversations with the staff and readings of some of the bills introduced since 1981 in this committee, that you and your colleagues are considering potential amendments to the Food, Drug, and Cosmetic Act and related statutes. Certain of these amendments I find quite attractive.

For example, provisions to encourage detailed characterization of risks to health from substances present in foods as additives or contaminants would be useful. My preceding remarks indicate that such risk assessment provides a desirable framework for critical review and interpretation of available data.

Congress should be careful, however, I believe, in making requirements for such analysis that the staff at FDA could not meet. In general, it is my impression that the FDA staff have utilized information pretty well in decisions about risk and safety for food contaminants. They have relied on action levels instead of trying to meet more stringent procedural and substantive requirements to set tolerance levels. In the nascent state of the art of risk assessment, and with realistic limits in the data, we must not paralyze the system through requirements for analysis.

The situation for food additives is quite a challenge. I think the general policy behind the General Food Safety clause and the Delaney clause of 1958 is a stiff and appropriate standard of safety for most food additives. Unfortunately, with the loss of innocence about no-effect thresholds and with the increasingly sensitive techniques for the detection of the presence of such substances in foods, we have some pretty difficult questions.

Congress dealt with this matter by exception in the cases of saccharin and nitrites during the 1977 to 1980 period. At this point we still do not know whether these situations are exceptional or whether the saccharin and nitrites cases signal a flow of similar problems.

Let me emphasize that there are some important lessons in the saccharin and nitrites cases. The saccharin debate was frustrating especially because of lack of data. Despite clearly positive bioassay results for bladder cancer in male rats, there was no clue to the mechanism of action. Saccharin itself seems an unlikely chemical carcinogen, and no known metabolic activation accounts for the apparent effects in male rats. The sex and organ specificity are unexplained, especially if a promoter role is the postulated mechanism. The human studies have been unimpressive, with conflicting claims based upon statistical dichotomization of results as positive or negative.

Even more frustrating, I think, to the Congress and to the rest of us, was the lack of any systematic data on the presumed health benefits from availability of saccharin. There was plenty of time for obtaining such data during the protracted review by FDA and the subsequent public debate. Had cyclamates still been available or Aspartame already been approved, Congress might have viewed the public clamor for a nonnutritive sweetener differently with regard to saccharin.

The nitrites case presents other lessons. Nitrites are natural constituents of foods, so that nitrites as food additives represent only about 15 percent of our intake of nitrites. There is no question that ingested nitrites can react with various amines to produce certain nitrosamines, which are widely accepted to be carcinogenic. However, FDA and the Department of Agriculture have no regulatory jurisdiction over what happens inside our gastrointestinal tracts.

When a report became available purporting to show increased occurrence of tumors in animals exposed to sodium nitrite, the FDA and the USDA mobilized to reduce and remove nitrites as food additives. Immediately a knotty legal and public health problem was noted. Nitrites, besides their coloring effects, really do protect against botulism, a deadly public health threat. No well-established alternative agent was available. At the same time, it was acknowledged by all that the nitrites levels utilized far exceeded the concentrations required to protect against botulism.

A major legal initiative within the administration was launched to try to determine whether the Delaney and General Safety clauses permitted slow banning of a presumed carcinogenic food additive. I might inject that this story reminded me of my father's accounts, as an oral surgeon to whom patients with troublesome extractions were referred by other dentists. After having the extraction and hearing the fee, the patient might remark, "But, doctor, it only took a few minutes." His reply would be, "Would you rather I did it slowly?" Well, if the nitrites were so great, why were we so patient with the hazard?

In the rush for the legal legerdemain, the FDA did not give adequate attention to scientific review of the report which triggered all of this action. It fell to the White House Science and Technology Policy office (OSTP) and others to recommend referral to an outside expert advisory panel. FDA did that, and the review panel some 18 months later reported that the study did not warrant the FDA's determination that nitrites had been shown to be carcinogenic.

One of the proposed amendments, Senator, calls for greater use of expert advisory panels by the Bureau of Foods. I think the nitrites experience provides good justification for what is a sound administrative step in any case, and a step strongly endorsed by our National Research Council report.

In closing, let me recommend that your committee consider incorporating language encouraging the review and analysis of direct health benefits of food additives, following the nitrites case. I noted a statement in the committee's April 20, 1982 print "that the scope of health benefits to be considered, the manner in which they are demonstrated, and the manner in which risks and benefits are compared are unresolved." There is no question that resolution will be difficult and contentious.

I believe it is unfair to make an already burdened agency responsible for such decisions, unless Congress provides clear guidance and unless the burden of proof is a stiff one and is laid clearly upon the manufacturer and users of such substances. The health benefit should be an important benefit, such as life-saving protection from botulism. The levels permitted in such cases should be limited to concentrations required for the desired effect. The availability of effective alternates should be considered, but we must remember the general problem that often we know too little about the potential adverse effects from the substitute.

The safety of our food supply is a precious feature of our society which the public rightly expects the Government and the manufacturers to take all necessary steps to maintain or enhance. For food additives, the introduction of concepts of balancing health benefits—let alone adequate safety—should be done with precision, not by opening unbounded loopholes.

Thank you very much for this opportunity to testify.

[The prepared statement of Dr. Omenn follows:]

TESTIMONY OF DR. GILBERT S. OMENN before
SENATE COMMITTEE ON LABOR & HUMAN RESOURCES

9 June, 1983 at HEARINGS ON SCIENTIFIC AND
PUBLIC POLICY ISSUES RELATED TO FEDERAL
FOOD SAFETY LAWS

Mr. Chairman:

I am very pleased to appear today before the Senate Committee on Labor & Human Resources on this panel with my colleagues, Dr. Joseph Rodricks and Dr. Reuel Stallones. My position is Dean of the School of Public Health & Community Medicine at the University of Washington in Seattle, where I am also chairman of the Department of Environmental Health and Professor of Medicine. During the Carter Administration I served as a deputy to Dr. Frank Press, the President's Science and Technology Adviser and Director of the Office of Science & Technology Policy, and then as an Associate Director of the Office of Management and Budget. In both of these positions I was involved in matters arising in or affecting the Food and Drug Administration.

I will address some of the broader aspects of qualitative and quantitative risk assessment; Dr. Rodricks will focus on applications of special importance at the FDA; and Dr. Stallones will describe the most important findings and conclusions of the recently-completed National Research Council Panel on Institutional Arrangements for Risk Assessment in the Federal Government. All three of us served on that Panel.

I will keep these remarks brief. A longer statement about general aspects of risk assessment have been provided to your staff and to those attending this Hearing. I trust that the supplementary testimony will be included in the Committee Report.

Definition of Risk Assessment

The term "risk assessment", according to the NRC Panel Report and many other studies, means the characterization of the potential adverse health effects from exposures of people to specific environmental hazards.

Thus, risk assessments include descriptions of observable health effects in epidemiologic, clinical, and toxicologic studies of particular agents; extrapolations from those results to predict the types and estimate the probability of health effects in humans under given conditions of exposure; judgments about the number of persons exposed at various concentrations and for various times and about the characteristics of those persons actually exposed; and analyses of the existence, nature, and magnitude of the public-health problems associated with such exposures, including explicit recognition of the uncertainties inherent in this process of inferring risk. Risks must be characterized both qualitatively and quantitatively.

Another way of describing the process of risk assessment is to list the four steps: (1) identification of potential hazard; (2) assessment of dose/response relationship; (3) analysis of exposures; and (4) characterization of risk.

Risk assessment can begin only after data have been obtained from laboratory, clinical, and field research on health effects and exposures, combined with empirical and theoretical studies of methods for extrapolation from observable effects at high doses to potential effects at lower doses. Risk assessment ordinarily should be completed before regulatory agencies, manufacturers, or others evaluate the "risk management" options and make their decisions on regulation, production, or use of particular substances.

Advantages and Limitations of Risk Assessment

The advantages are three:

1. Risk assessment provides a framework for explicit analysis of the data on a particular substance. Both negative and positive results in various assays, full descriptions of carcinogenic, mutagenic, teratogenic, organ-specific, and general toxic effects, and detailed information about possible mechanisms of action can be reviewed critically.

2. Risk assessment highlights the importance of dose of exposure. Nature, sources, and time-course of exposures must be considered, as well as the susceptibility of various subgroups in the population, defined by age, sex, co-existing exposures, illnesses or behavioral patterns (such as cigarette smoking), and other factors.

3. Risk assessment helps to differentiate the "biggies" from marginal or negligible hazards. Those responsible for assuring "safety" through their risk management decisions need informative and intelligible characterizations of risk as inputs for such decisions about safety.

Three kinds of limitations must be emphasized:

1. Risk assessment cannot provide new results when research results are lacking or conflicting. Risk assessment provides a critical framework for interpreting results and also identifying gaps in available results. Nevertheless, risk managers often must make decisions based upon the available evidence; it is not fair to blame the messenger when the evidence is limited or poor. Sometimes a judgment will be made that there is time

to seek better evidence (especially when exposures are limited, or better substitutes not available). Sometimes the risk managers will decide that protective steps would be prudent. We must not confuse the risk assessment and risk management functions.

2. Characterization of risk at low-dose exposures requires extrapolation from observable effects in animals or highly exposed workers. Effects that can be observed at a statistically significant frequency in groups of 50 rats or in relatively small numbers of workers must be extrapolated to probabilities of adverse effects occurring when many thousands or millions of people are exposed to air pollutants or food additives or water contaminants throughout this country. We are forced to make models of the dose-response curve down to very low doses. Too often in the characterization of risk we are dealing with a "black-box" situation comprising measured exposures, observed effects, and models of extrapolation. We have high hopes that more detailed study of specific compounds for the mechanisms of action in producing cancers or birth defects or other damage will refine this extrapolation process, but we must not fool ourselves by thinking that such extrapolation will become unnecessary.

3. The linear dose/response extrapolation model, widely utilized and widely accepted, has the inevitable consequence that there will be some probability of risk at all doses of exposure greater than zero. For years we ignored this problem by assuming that if a substance were "below any detectable level" the risk could be considered functionally equivalent to zero exposure. With stunning advances in analytical chemistry, our powers of detection have been so enhanced that this convenient and pragmatic approach does not work. The FDA has been grappling for several years with policies and regulations about this problem of "sensitivity of detection". A corollary fiction is the "no-effect threshold" approach. For many health effects--just as in engineering bridges--it is assumed that a margin-of-safety can be introduced that reduces risk essentially to zero. Safety engineers are often hostile to discussions about low-probability events; they rely on good principles of design and construction and expect others to be satisfied that the results assure "safety", even though there may well be residual risks. The FDA uses this concept extensively in determining whether action levels are exceeded in various cases of food contaminants (inadvertent additives to food supply). For carcinogens, however, and particularly for carcinogenic food additives deliberately introduced into the food supply no such tolerance for very low dose, very low probability effects is currently permitted by law. The linear dose-response model and everything we know about direct-acting carcinogens suggest that no absolutely safe non-zero dose exists--or, if it does, that we cannot prove it, given individual differences in susceptibility and practical sample sizes. Ironically, the same arguments apply for mutagens,

teratogens, irritants to the lung, and other health effects besides carcinogenesis, even though assumptions of no-effect thresholds are still being made for these effects. Of course, any particular hazardous substance may produce a variety of health effects. These considerations provide the impetus for proposals to define "insignificant risk" or "negligible risk" or "adequate safety".

It is my view that the estimation and characterization of risks should be the tasks of the scientists and risk assessors, but that the conclusions of adequate safety or insignificant risk must be drawn by policy officials, manufacturers, and consumers responsible for those risk management decisions--guided by the statutes and other actions of the Congress.

Some Remarks About the Food Safety Laws

I know, Mr. Chairman, from conversations with your staff and from reading some of the bills introduced for consideration by this Committee, that you and your colleagues are discussing a number of amendments to the Federal Food, Drug, and Cosmetic Act and related statutes.

Certain of these amendments I find quite attractive. For example, provisions to encourage detailed characterization of risks to health from substances present in foods as additives or contaminants would be useful. My preceding remarks indicate that such risk assessment provides a desirable framework for critical review and interpretation of available data. However, the Congress should be careful, I believe, in making requirements for such analysis that the staff at FDA could not meet. In general, it is my impression that FDA staff have utilized information well in decisions about risk and safety for food contaminants. They have relied upon action levels, instead of trying to meet the more stringent procedural and substantive requirements to set tolerance levels. In the nascent state of the art of risk assessment and with realistic limits in the data, we must not paralyze the system through requirements for analysis. The Report from the Office of Technology Assessment in December, 1979, dealing with "Environmental Contaminants in Food" represents a fine framework for consideration of possible changes in the Act and possible early-detection of environmental contaminants in the food supply.

The situation for food additives is more challenging. I believe that the Congress has established through the General Food Safety Clause and the Delaney Clause of 1958 a stiff and appropriate standard of safety for most food additives. Unfortunately, with the loss of innocence about no-effect thresholds and with the increasingly sensitive techniques for detection of the presence of such substances in foods, we must face some pretty difficult questions. Congress dealt with this matter by exception in the cases of saccharin and nitrites during the 1977 to 1980 period. A moratorium was voted against regulatory control of saccharin uses, a similar moratorium was threatened against regulatory phase-down of nitrites, and studies by the National Research Council were mandated. At this point, we still do not know whether these situations are exceptional or whether the saccharin and nitrites cases signal a flow of similar problems.

There were important lessons from the saccharin and nitrites cases. First, the saccharin debate was frustrating especially because of the lack of data. Despite clearly positive bioassay results for bladder cancer in male rats, there was no clue to the mechanism of action. Saccharin itself seems an unlikely chemical carcinogen and no known metabolic activation accounts for the apparent effects in male rats. The sex and organ specificity are also unexplained, expecially if a promoted role is the postulated mechanism. The human studies have been unimpressive, with conflicting claims based upon statistical dichotomization of "positive" and "negative" results. Even more frustrating was the lack of any systematic data on the presumed health benefits from availability of saccharin. There was plenty of time for obtaining such data during the protracted review by FDA and the subsequent public debate. Had cyclamates still been available or Aspartame already been approved, the Congress might have viewed the public clamor for a non-nutritive sweetener differently with regard to saccharin.

The nitrites case presents other lessons. Nitrites are natural constituents of foods, so that nitrites as food additives represent only about 15 percent of our intake of nitrites. There is no question that ingested nitrites can react with various amines to produce certain nitrosamines which are widely accepted to be carcinogenic. However, FDA (and USDA) have no regulatory jurisdiction over what happens inside our gastrointestinal tracts! When a research report became available purporting to show increased occurrence of tumors in animals exposed to sodium nitrite, the FDA and the USDA mobilized to reduce and remove nitrites as food additives. Immediately a knotty legal and public health problem was noted. Nitrites, besides their coloring effects, really do protect against botulism, a deadly public health threat, and no well-established alternative agent was available. At the same time, it was acknowledged by all that the nitrites levels utilized far exceeded the concentrations required to protect against botulism. A major legal initiative within the Administration was launched to try to determine whether the Delaney and General Safety Clauses permitted "slow banning" of a presumed carcinogenic food additive. This period reminded me of my father's stories about a few patients--referred to him by other dentists for particularly troublesome extractions--who remarked after the extraction about his fee, saying "But, Doctor, it only took a few minutes". And his reply, "Would you rather I did it slowly?" Well, for nitrites, the proposal was to do it slowly!

Unfortunately, in its rush for such legal legerdemain, FDA did not give adequate attention to the scientific review of the report which triggered all this action. The White House Office of Science & Technology Policy and others strongly recommended referral to an outside expert advisory panel. FDA did so, and the review panel some 18 months later reported that the study did not warrant FDA determination that nitrites had been shown to be carcinogenic. One of your proposed amendments, Mr. Chairman, calls for greater use of expert advisory panels by the Bureau of Foods. I think the nitrites experience provides good justification for what is a sound administrative step in any case, a step strongly endorsed by our NRC Report.

Let me close by recommending that your Committee consider incorporating language encouraging the review and analysis of direct health benefits of food additives, following the nitrites case. However, I noted the statement in the Committee's April 20, 1982, print (p.7) that "the scope of health benefits to be considered, the manner in which they are demonstrated, and the manner in which risks and benefits are compared are unresolved". That resolution will be difficult and contentious. It is unfair to make an already-burdened agency responsible for such decisions unless Congress provides clear guidance and unless the burden of proof is a stiff one and is clearly laid upon the manufacturer and users of such substances. The health benefit should be an important benefit, such as life-saving protection from botulism. The levels permitted in such cases should be limited to concentrations required for the desired effect. The availability of effective alternates should be considered, but the general problem that we often know too little about potential adverse effects from the substitute must be considered, too.

The safety of our food supply is a precious feature of our society which the public rightly expects the government and manufacturers to take all necessary steps to maintain or enhance. For food additives, any introduction of concepts of balancing health benefits, let alone "adequate safety", should be done with precision, not by opening unbounded loopholes.

Thank you, Mr. Chairman, for inviting me to testify.

Supplement on General Aspects
# of Risk Assessment
for
Testimony June 9, 1983
before the Committee on Labor and Human Resources,
U.S. Senate Hearings on
Risk Assessment and Food Safety Laws

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Characterization of Risk: A Crucial Aspect of Risk Assessment for Environmental Policy Making

Presented at the U.S./F.R.G. Binational Workshop on Risk Management, National Science Foundation, Washington, D.C., April 25-28, 1983

Risk assessment is with us, both qualitative and quantitative risk assessment. The important questions address how, when, and by whom risk assessment should be done. Those who claim that risk assessment should not be used or cannot be used fly in the face of actual experience in our regulatory agencies, particularly at FDA and at EPA.

The literature on methodology and on applicability of risk assessment has been growing rapidly, with much useful case material now available. For the policy-oriented reader, I generally recommend the following sources: The OTA Report, "Assessment of Technologies for Determining Cancer Risks from the Environment," especially chapter 5 (1); Lave's books, The Strategy of Social Regulation: Decision Frameworks for Policy (2) and Quantitative Risk Assessment in Regulation (3); a paper in Science by Ricci and Molton for an introduction to legal issues and precedents (4), the Calkins et al paper from the Office of Science and Technology Policy (OSTP), for a concise summary of my views and recommendations and for references to the risk assessment guidelines of each of the regulatory agencies and of the Interagency Regulatory Liaison Group (5); and the recently released report from the National Academy of Sciences on Risk Assessment in the Federal Government: Managing the Process, which seeks to clarify the distinctions between risk assessment and risk management decisions (6).

As a personal note, I might add that my combined background in scientific research and in clinical medicine has provided a very helpful perspective, in fact something of an analogy, to the scientific and regulatory aspects of risk assessment and risk management. Scientists have the luxury of framing hypotheses and

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See Appendix I on Applications of Quantitative Risk Assessment pursuing experimental evidence, in principle without time limits. It is commonplace for a scientific review panel addressing an urgent policy matter to conclude that "more research is needed." A physician, on the other hand, is very much a decision-maker and must make decisions on someone else's schedule. Some of the most important decisions in medicine focus on whether or not action is required at that moment and, if not, what sorts of information can be obtained, in what sequences and with what urgency, to permit a better informed decision later. Furthermore, the consequences of actions taken need to be anticipated. Policy makers are in quite a parallel position.

THE SETTING

During the past decade, hazards and potential hazards to human health from exposures in the many facets of our environment have received much public and governmental attention. Air pollution, water pollution, pesticides, food additives and food contaminants, sewage, chemical wastes, radioactive wastes, chemical by-products from energy development, and cigarette smoking all have been targets of hearings, laws, regulations, public information campaigns, and litigation. As scientists and as public officials, we have a responsibility to distinguish the most important hazards from those which are less important or marginal.

An important challenge for policy makers lies in the widespread misperception among the public and even among scientists that practically every chemical will prove carcinogenic or mutagenic or otherwise hazardous if tested long enough and at high enough doses. A National Journal article on the saccharin debate in Congress five years ago was embellished with a border of mice all 'round the page--dead mice, of course, with obvious tumors; under each was given the cause: saccharin, air, fried chicken, tea, malted milk balls, water, blueberry waffles, coffee, lasagna, tobacco, and--aphrodisiacs! Similarly, the Community Nutrition Institute and Food Marketing Institute closed their 1981 conference report "Focus on Food Safety" with a sorrowful tale depicted in Figure 1 (7).

It is not true that all chemicals will be positive if tested sufficiently. In fact, only a minority, probably 20 percent or less, will be positive in standard bioassays and screening tests. We have a long way to go in regaining public confidence and public interest. We must overcome the ennui that seems to be paralyzing action among those who have learned that charbroiled hamburgers, broiled fish, and fresh fruits all have been shown to contain mutagenic or carcinogenic substances. Ironically, more recent work from excellent research in Japan shows that the diet contains many anti-mutagenic compounds, as well, which counteract or inactivate the mutagen previously described in other foods. Common vegetables are especially active anti-mutagens (8,9) reinforcing the traditional dietetic recommendations for "balanced meals".

A FRAMEWORK FOR REGULATION

Table 1 outlines the framework for Federal decision-making in the United States. The major tasks of identification, characterization, and control of potential human mutagens and carcinogens are divided into two stages: first, the scientific work and scientific review, and, second, the regulatory process which must decide upon appropriate actions (5). Priorities are essential for a well-organized research program and for human and financial investments in the assessment or characterization of risk. Priority-setting is even more important for the arduous decision processes in the regulatory phase.

Identification of Potential Hazards

Let us review briefly the framework. The first task, identification of compounds with mutagenic or carcinogenic or other toxic activity, seems relatively straightforward. Nevertheless, we found that it was necessary to define rules of evidence and build healthy respect for objective scientific analysis. The most difficult problem is how to handle conflicting data. For example, one test may show a compound to be "positive", while one or more other tests show no statistically significant effect. It is essential to understand that there is no qualitative difference between "positive" and "negative" results. These terms apply, according to statistical criteria, to the quantitative results in numbers of animals with tumors or numbers of humans dying of lung cancer or some other measured effect in the exposed or treated group, compared with the frequencies of the same effects in the "control" group. The statistical test assesses whether or not the difference in frequency is likely to be due to chance variation or is too large to be likely to be due to chance alone. Obviously, the number of animals, the frequency in the control group, and the statistical test applied are crucial variables. Even when the incidence of tumors is none (no additional tumors compared with the controls) in 100 exposed animals, the 99 percent confidence limit permits us to conclude only that the actual risk of cancer excess is no more than 4½ percent (see reference 1, p. 164 corrected). It is essential to be clear whether the estimated risk or incidence is an observed frequency, a "best estimate," or an estimate of the "upper bound" defined statistically by a 95 percent or 99 percent confidence limit.

Some regulators or activists have proposed that any positive evidence must be considered a basis for regulatory action as a precaution to protect public health. I believe that every test, whether positive or negative, must be reviewed in detail for its design, conduct, and biological--as well as statistical--meaningfulness. Biologic features of a positive outcome include appropriate dose-response and time-dose relationships and absence of signs of non-carcinogenic toxicity from high doses. When evidence of carcinogenicity is found only at toxic doses, such evidence should be rejected as demonstrating carcinogenic potential for humans if it seems reasonable to conclude that the toxic effect noted could have created a unique susceptibility to cancer in the animal population that would not be encountered in human exposures. An example is the role of a chemical such as nitrilo-triacetic acid which becomes insoluble at high doses, leading to crystal and stone formation in the urinary tract, and causing bladder tumors only at those highest doses. Regulatory action should proceed only when the preponderance of all available evidence points toward carcinogenicity. For other health effects, there is often dispute about whether an effect is adverse or, if adverse, significant clinically. We shall cite examples below from EPA actions on photochemical oxidants and on lead in air.

I strongly recommend that all agencies supporting animal tests or in vitro tests and using such results for regulatory action should adopt uniform testing guidelines or protocols. The European Economic Community has undertaken to do so, as did the Interagency Regulatory Liaison Group in this country. Obviously, periodic updating of the guidelines must be an integral feature.

This process of identifying potential hazards from screening tests, animal bioassays, clinical measurements, and epidemiological studies seems simple enough. However, we need only recall the nitrites case, or a host of other controversial problems in regulatory science, to recognize that pressures for action--either for public health or for political reasons--may swamp the objective and logical review of the scientific evidence.

Characterization of Risk

The second task, characterization of risk, represents the greatest challenge to the scientific community. I much prefer the work "characterization" instead of "quantitation" of risk, because both qualitative and quantitative information must be brought together in the assessment of risk for humans. Careful description of the health effect or, more often, the multiple health effects of a particular agent is essential. Such descriptions are too often neglected in a rush to extrapolate selected observations to some generalized quantitative risk estimate. As shown in Table 1, there are three main elements in the characterization of risk.

First, there is the matter of relative potency, the dose/ response relationships. Several different kinds of responses may need to be analyzed for a particular agent or exposure. Thus far, most attention has been focused on carcinogenic activity, but efforts to apply risk assessment to mutagenic, teratogenic, and other adverse reproductive outcomes are notable (9,10,11). As testing protocols are standardized and more widely utilized, there will be more and more basis for comparison of data on different chemicals from the same test system. Estimates of relative potency are feasible within a single test system. Results may be expressed as dose required to cause 50 percent of animals to have a particular type of tymor, with adjustments according to life table analyses (12,13). Alternatively, potency may be expressed in terms of probability of tumors or cancer deaths or other effects per unit dose of the compound; EPA has used $\mu g/m^3$ as a unit dose for potential carcinogens in water and air (14).

Beginning with bioassays in animals, we must utilize two kinds of extrapolation to estimate potency for humans: first from high dose to low dose effects in animals, and then from low doses in animals to low doses in humans. Several models of extrapolation from high doses have been proposed and compared (1).

Estimated effects at very low doses are sensitive to the choice of model for extrapolation, whereas most of the models fit the data in the observed high dose range about equally well. The linearized multistage model developed by Crump et al (15) has been adopted by EPA and has the advantage of being compatible with current thinking about the multiple stages of initiation and progression of tumors from a biological point of view. The linearized multistage model has the further advantage of utilizing all the data points, in those experiments which have more than one dose with interpretable results. From a policy point of view, I support the decision of EPA to use this model and, more importantly, to use one model consistently.

Determination of effective dose is not a simple matter. Fortunately, more sophisticated analyses are being carried out, which move inside the "black box" of statistical associations and mathematical extrapolations to examine biochemical mechanisms. A good example is the paper of Hoel et al (16) in which DNA-adduct concentrations are utilized as the effective doses for genotoxic agents and other non-linear kinetic processes such as saturation of detoxification, adduct excision, or other DNA repair mechanisms. It should be noted, of course, that the usual mathematical models for extrapolation to very low doses may overestimate risks by large margins when these kinds of non-linear processes are involved. Analogous efforts to establish effective doses in target tissues have been mounted in studies of germinal mutations (11).

Extrapolation from animals to humans raises many problems. Since rodents are much smaller, a factor is needed for scaling up. Four different factors have been utilized: mg/kg/day; ppm; mg/m^2/day; and mg/kg/lifetime; the relative risk from these different scaling factors from mouse to human rises in order listed from 1 to 6 to 14 to 40 fold (see OTA, reference 1, p. 170). The lifetime denominator is probably least justifiable, given differences in rates of growth, metabolism, and cell division.

However, from a policy point of view, again what is critical is that the same factor should be employed, to permit ranking of relative potency.

Another common problem is the discrepancy of results between species or strains of animals (17,18). For example, in a series of 98 chemicals which were "positive" in NCI bioassays in either rats or mice or both species, 54 were positive in only one species or the other (17). In the absence of firm evidence that the species with positive test results is strikingly different from humans in metabolism of the chemical or susceptibility to its effects and that the species with negative test results is similar, it is generally agreed that the "sensitive" species should be used as the basis for extrapolation. Laboratory animals are highly inbred, thus showing much intra-species variability than humans. The negative results can be taken into account in the qualitative assessment of the weight of evidence. Also, Ames and his colleagues have found that differences between reported positive and negative results often reflect differences in number of animals tested and in dose range utilized, so that 95 percent confidence limits often overlap both the "positive" and "negative" results.

Extrapolation to quantitative estimates of potency in humans involves many more assumptions, of course. In some cases there may be useful epidemiological information. Even in these cases, often based on poorly controlled occupational exposures, there is difficulty in extrapolation from high dose to low dose and from workers to other human population groups. Such cases should be reviewed very carefully to validate the philosophy and policy described here. Epidemiological results can indicate doses at which effects begin to become detectable in humans, or doses at which effects still are not detectable. As in animal bioassays, it is essential to be clear about the statistical treatment applied to what is often a very small difference in observed frequencies. Often, the upper 95 percent confidence limit is used to estimate the risk which may be associated with an observed "positive" effect, while the lower 95 percent confidence limit is used to estimate a dose that can be tolerated with no effect. The "best estimate" would fall in the mid-zone of these very different estimates.

Second, the exposures to humans must be characterized carefully. In general, information about exposures is woefully inadequate. It is essential to determine the sources, prevalence, levels, and time-course of exposures. Cooperation from industry is crucial to determine how many people were or are exposed in the various classes of exposures and to generate productive labor/management efforts. Also it is necessary to check for impurities and contaminants of the chemical and for environmental alterations. Finally, it is useful to analyze existing data in light of information about reductions or increases in exposures since the time of the studies. These descriptions of health effects and of exposures must be combined with quantitative estimates of potency and exposure to permit quantitative risk assessment.

Third, characterization of risk should examine differences in susceptibility in the human population. Age, sex, genetic predisposition, exposure to other chemicals, and important lifestyle factors such as smoking deserve attention. Biological variation may involve the metabolic activation and inactivation of the compound, inherited or exogenous factors which enhance tumorigenicity, repair mechanisms, and anti-tumor metabolites, including anti-oxidants.

The laws governing the regulatory programs in the United States for control of air pollution and protection of workplace safety and health explicitly require EPA and OSHA to set standards so as to protect the most susceptible groups or individuals in the population (19,20). In standard-setting under section 109 of the Clean Air Act, for example, EPA in 1978 gave explicit attention to the 3-5 percent of the population with asthma, bronchitis, or emphysema in establishing the revised air quality standard for photochemical oxidants (ozone), aiming to protect 99 percent of this subgroup against reversible respiratory symptoms (21). A similar process generated an air quality standard for lead which was directed at protecting 99.5 percent of exposed children (22). In this standard, the target was to prevent any increase in blood lead level or in the biochemical marker for lead exposure, erythrocyte protoporphyrin levels. "Safe" levels allowed only very small exposures from airborne lead, since 80% of lead exposures come from other media not addressed in that ambient air quality standard. It is a matter of judgment whether 99.5 , or 99, or 95, or 99.8, or some other percentage should be protected, but it is a practical fact that individual variation is so significant that protection of everyone must be considered a rhetorical goal, not a feasible regulatory objective. These examples also serve to illustrate that there are other important health effects, besides carcinogenicity (see Table 2). These other effects share the problems of extrapolation to low doses and of individual variation in susceptibility. Furthermore, they share the property that no safe threshold for the population can, in reality, be demonstrated.

Unfortunately, the research work usually has not addressed this variable of differential susceptibility in any detail. Research clues from pharmacogenetics and ecogenetics are many (see Table 3) and have been reviewed elsewhere (23,24,25). In the past two years, policy and research interest in this area has increased markedly, with careful studies of asthmatic adolescents as one good example (26) and with numerous conferences highlighting genetic and physiological differences.

Priorities for the stage I review, the scientific review, must be set, because of the large number of chemicals now on the market and the steady flow of new chemicals. For testing, the highest priority should be given to chemicals for which preliminary analysis suggests that regulation may be indicated but for which existing data are too uncertain to justify immediate action.

These chemicals generally would include those that have a high potential for carcinogenicity, based upon structural similarities or results from short-term *in vitro* tests, but have had minimal prior testing; ones that offer substantial consumer benefits; and those that do not have readily available means for control. These criteria have been applied effectively in the Chemical Selection Process of the National Toxicology Program, in which the regulatory and research agencies cooperate (27). We expect results from *in vitro* screening tests to supplant long term animal bioassays as decision rules are adopted (28,29). Detailed characterization of risk is mandatory for any chemical that has been identified as a potential carcinogen for humans. It should be done first for those with greatest apparent potency and greatest potential human exposure.

Characterization of risk in complex situations can be illustrated with the EPA standard-setting for airborne lead. Figure 2 shows the relationship of adverse or physiological responses to dose in the most susceptible persons in the population, i.e. these doses are the blood lead concentrations at which susceptible individuals begin to show the response cited (30-32). From empirical observations and from numerous investigations (Table 4) it is clear that young children constitute the most susceptible easily identified subgroup in the population; thus, the EPA standard was directed at protection of this subgroup. Other subgroups, of course, could have been chosen, such as inner city children, or children who have iron-deficiency anemia, or perhaps children with learning disabilities. Prevalence studies demonstrate that black inner city children have the highest prevalence of elevated blood levels of lead (greater than 30 µg/dl) which may be associated with anemia (Table 5). The steps that EPA then utilized in proposing a standard are outlined in Table 6: defining the sensitive population; determining the critical health effect to be prevented; estimating the threshold for that effect in sensitive individuals;

postulating the contribution of airborne lead to the blood lead; and finally calculating the limits to air lead levels consistent with restriction of the airborne increment in blood lead levels. Table 7 shows the way in which EPA selected relatively protective values at several of these steps in the calculation, and Figure 3 shows how different the final standard could be when calculated within the estimates in Table 7; the final airborne lead standard could have ranged from 1.5 $\mu g/m^3$ to 5 $\mu g/m^3$ on these variables, alone.

The meteorological model utilized to estimate exposures from the airborne lead via inhalation into the children's lungs becomes a significant variable, as well. Table 8 shows how exposures at various distances from a smelter fall off from the 1.5 $\mu g/m^3$ concentration in the effluent. Analogous calculations would be required to relate traffic density and housing areas to appropriate estimates of exposures and of numbers of persons likely to be affected. Finally, Figure 4 shows the difference in compliance with a standard that averages airborne lead levels (top) versus compliance with a standard that puts a ceiling on the peak concentration.

The uncertainties and the technological and exposure consequences of all the steps in this process should be made explicit. Even this discussion represents considerable simplification, since others might prefer to focus attention on neurobehavioral effects of lead on learning or on cancer risk from lead compounds, neither of which was addressed in this approach to standard-setting.

The Regulatory Phase

The second stage or regulatory phase of the framework (Table 1) has been under intense review in the last several years in the United States. President Ford instituted regulatory impact analyses. President Carter proposed extensive regulatory reform measures and ordered in December 1978, that all major regulations be subjected to economic analyses and a new layer of review by a multi-agency body chaired by a member of his Council of Economic Advisers. (I served on that Regulatory Analysis Review Group). The Reagan Administration expanded that central review process and required that cost-benefit analyses be done. These pressures resulted in more care in the selection of targets for full regulatory action and more analysis of the cost-effective alternatives for achieving similar objectives. In the past two years, however, there have been very few actions against chemical hazards.

There is still a need for better coordination across agencies and even within agencies regulating a given chemical in different media or from different sources. For example, EPA's regulations for lead in air ignored important sources of lead in food and other exposures. All of the reductions in blood lead required to protect health were to be achieved by reductions in air lead sources alone (32). It should be a matter of philosophy and policy that the government has a responsibility to protect health and welfare from environmental hazards in ways that are both effective and efficient.

Table 9 outlines a scheme for setting the priorities for regulation. The steps listed are all feasible: (1) identification of those chemicals with strong evidence for carcinogenic activity, as published and documented by the International Agency for Research on Cancer (IARC) (37) and by the National Toxicology Program in the United States (34); (2) estimates of relative potency--this step requires detailed review of the data for those compounds which have been tested in comparable test systems; (3) estimates of current production and sources (35), with care to assess impurities and contaminants; (4) characterization of the exposures for humans--nature, routes, time-course, and levels; (5) data from actual measurements of human body burdens, available in tabular form from the EPA (36); and (6) an explicit plan to attack these hazards according to their relative potency and exposure levels, i.e. according to their relative risk, combined with qualitative assessment of the strength of the evidence and information about substitutes and alternative means for reducing exposures.

Another important policy question involves the institutional arrangements for carrying out and inter-relating the scientific reviews and the regulatory analysis. Within the government, different agencies have evolved different relationships. FDA carries out its own risk assessments and has a long tradition of balancing risks and benefits for drugs--but not for food additives. EPA has a centralized health effects assessment group which performs quantitative risk assessment for the various program offices. OSHA relies heavily upon NIOSH for criteria documents and is beginning to do more analytical work. All of these agencies work through the National Toxicology Program with NIH research institutes to set priorities for testing chemicals and to develop better tests. Several bills have been introduced in the Congress to separate scientific review from regulatory agencies' activities and to centralize the leadership for such reviews in the Office of Science and Technology Policy, or the National Academy of Sciences, or some new Science Panel.

A National Academy of Sciences panel (6) has reviewed these and other potential arrangements for enhancing the scientific quality of regulatory decision-making and for separating and linking the risk assessment and risk management responsibilities of federal agencies. That Panel, on which I served, recommended three complementary avenues to improved risk assessment in the regulatory process:

1. "...That regulatory agencies take steps to establish and maintain a clear conceptual distinction between assessment of risks and consideration of risk management alternatives; that is, the scientific findings and policy judgments embodied in risk assessments should be explicitly distinguished from the political, economic, and technical considerations that influence the design and choice of regulatory strategies."

2. "...That uniform inference guidelines be developed for the use of federal regulatory agencies in the risk assessment process."

3. That Congress establish a Board on Risk Assessment Methods "to perform the following functions:

(1) To assess critically the evolving scientific basis of risk assessment and to make explicit the underlying assumptions and policy ramifications of the inference options in each component of the risk assessment process.

(2) To draft and periodically to revise recommended inference guidelines for risk assessment for adoption and use by federal regulatory agencies.

(3) To study agency experience with risk assessment and evaluate the usefulness of the guidelines.

(4) To identify research needs in the risk assessment field and in relevant underlying disciplines." (6, pp. 7-8).

CONCLUSION

Interest in the techniques and assumptions, the data and models, and the embedded policies and values in risk assessment is widespread and growing. The relevant federal agencies are deeply engaged, and the last three Administrations have pushed hard for better and more explicit analytical work in the regulatory arena. I am confident that the same framework we have described for assessment and regulation of potential carcinogens (see Table 1) will be applied to mutagens, teratogens, and agents causing other adverse health effects. The heart of the framework is the combination of qualitative and quantitative characterization of the risks.

We should be clear that there is much to be learned about the doing of risk assessment and the most appropriate assumptions and extrapolations. Policy guidance on such matters as testing guidelines, statistical treatment, choice of mathematical model for extrapolation to low doses, and choice of scaling factor for extrapolation from animals to humans can enhance the usefulness of risk assessment and remove some of the non-scientific, spurious discrepancies which are wrongly attributed either to the scientific evidence or to the methodologies of risk assessment. However, we should recognize that it is a long and uncertain leap from qualitative and quantitative risk assessment to politically and socially acceptable risk management decisions.

APPENDIX I

APPLICATIONS OF QUANTITATIVE RISK ASSESSMENT

Examples are categorized here, as summarized by Dr. Elizabeth Anderson of EPA (14).

1. Balancing Risks and Benefits

FIFRA, TSCA, and the Drinking Water Act all require balancing risks and benefits. Instructive examples can be cited from the pesticide program. In the case of chlorobenzilate, the qualitative weight of evidence was not strong, and the quantitative risk, assuming that the compound is indeed a carcinogen for humans, was low (2×10^{-6}) for nationwide populations. For applicators the estimated risk was 200-500 times higher. There were no ready substitutes for this compound on citrus. The decision was made to continue registration on the basis that benefits outweighed risks, but to apply additional labeling requirements in an effort to protect applicators from high risk.

In the case of amitraz, qualitative evidence was weak, but limited to a single bioassay study, and quantitative estimates of potential risk were low. The application was for new registration for use on pears and apples. The decision permitted conditional three-year registration for use on pears, for which there was no substitute, but denied use on apples, for which there are substitutes. Additional testing was required for permanent registration.

Finally, for chlordane/heptachlor, qualitative evidence was considered very substantial, based upon repeated positive tests in a series of animal studies. Population risk was high (10^{-4}), since everyone has a body burden due to bioaccumulation. After three years of hearings, most uses were cancelled; underground use for termite control was permitted, however, because exposures were limited and benefits were judged to outweigh risks.

2. Setting Target Levels of Risk

FDA has used a target level of risk of 10^{-6} to define contaminant levels of carcinogens in animal foodstuffs. EPA has used this approach when it must be decided when a control program is "adequate". Examples include target levels for carcinogens in water as guidance to the states under section 304 of the Federal Water Pollution Control Act; acceptable levels of a carcinogenic contaminant in the pesticide treflan under FIFRA; a guideline for exposure to radioactive transuranium elements; and target levels for cleanup of uncontrolled waste sites and disposal of hazardous wastes.

3. Setting Priorities for Program Activities

The Office of Air Programs has utilized reports from the carcinogen assessment group both to determine which potentially toxic chemicals should be listed under section 112 of the Clean Air Act and to decide which ones should be regulated after a full risk assessment. Descriptions of the weight of evidence and calculations of carcinogenic risks associated with unit doses provided a rough index of the potency of the pollutant, to be combined with information about exposure levels by source.

4. Estimating Residual Risks

Risk assessment has been used also to estimate risks remaining after application of Best Available Technology or some other control measure. In response to a petition that the EPA regulate vinyl chloride further after the initial regulatory action, EPA estimated residual risk and compared that risk with risks from other air pollutants which have not yet been regulated. This was done both for maximum exposures groups and for average exposure groups. It was clear that after initial regulation, vinyl chloride represented a much lower risk than arsenic, benzene, cadmium, or coke ovens. The agency chose to direct its efforts to the greater hazards.

This matter of significance of risk is certain to become a more and more important policy and judicial matter. In reviewing the benzene standard, the Supreme Court ordered OSHA to develop better evidence of the risks of exposure, noted that a "safe workplace" need not be construed to be a "risk-free" environment, and argued that if OSHA were correct in insisting that it need not characterize a risk as significant in order to proceed with regulation, then the statute might be unconstitutional as an overly "sweeping delegation of legislative power" (see 4, 37).

Quantitative estimates of risk often are stated in terms so precise as to defy credibility. Statistical descriptions of uncertainty may be lost to the fine print. Much more important, the risk is estimated with too many significant figures, for example, 2.43×10^{-5}, or 15.7 excess cancer deaths. Such numbers should be rounded off to 2×10^{-5} and 10-20 deaths to be consistent with the significance of the numbers in the original data. Whenever I see numbers in scientific or medical articles or in policy documents estimating risks, benefits, or costs with excessive precision, I conclude that the authors simply plugged data into equations and read results off calculators or computers without giving adequate thought to the meaningfulness of the numbers. Unfortunately, the reviewers and editors often fail to object.

REFERENCES

1. Office of Technology Assessment (U.S. Congress): Assessment of Technologies for Determining Cancer Risks from the Environment. June, 1981.

2. Lave LB: The Strategy of Social Regulation: Decision Frameworks for Policy. Brookings Institution, Washington, DC, 1981.

3. Lave LB (Ed): Quantitative Risk Assessment in Regulation. Brookings Institution, Washington DC, 1982, 264 pp.

4. Ricci PF, and Molton LS: Risk and benefit in environmental law. Science 1981 4 Dec; 214:1096-1100.

5. Calkins DR, Dixon RL, Gerber CR, Zarin D, and Omenn GS: Identification, characterization, and control of potential human carcinogens: a framework for Federal decision-making. J Natl Cancer Inst 1980 Jan; 64:169-175.

6. National Research Council: Risk Assessment in the Federal Government: Managing the Process. National Academy Press, Washington, DC, 1983, 189pp.

7. Community Nutrition Institute/Food Marketing Institute: Proceedings, 4th National Food Policy Conference: Focus on Food Safety, Washington, DC, 7-8 April, 1981, back inside cover.

8. Kada T, Morita K, and Inoue T: Anti-mutagenic action of vegetable factor(s) on the mutagenic principle of tryptophan pyrolysate. Mut Res 1978; 53:351-353; Kada T: Mechanisms and genetic implications of environmental antimutagens. Abst, Proc 3rd Intl Conf Environmental Mutagens, Tokyo, 21-24 Sept., 1981, p. 149.

9. Omenn GS: Environmental risk assessment: relation to mutagenesis, teratogenesis, and reproductive effects. J Amer Coll Tox 1983; 2:113-123.

10. Bloom AD (Ed): Guidelines for Studies of Human Populations Exposed to Mutagenic and Reproductive Hazards. March of Dimes Birth Defects Foundation: New York, 1981.

11. EPA: Assessment of Risks to Human Reproduction and to Development of the Human Conceptus from Exposure to Environmental Substances. Oak Ridge National Laboratory: ORNL/EIS-197, EPA-600/9-82-001, February, 1982.

12. Ames BN. Identifying environmental chemicals causing mutations and cancer. Science 1979; 204:587-593.

13. Ames BN. Mutagens, carcinogens, and anti-carcinogens. IN Genetic Toxicology, An Agricultural Perspective. RA Fleck and A Hollaender (eds). Plenum, New York, 1982, pp. 499-508.

14. Personal communication, Dr. E. Anderson (1982).

15. Crump KS, Hoel DG, Langley CH, and Peto R: Fundamental carcinogenic processes and their implications for low dose risk assessment. Cancer Res 1976 Sept; 36:2973-2979.

16. Hoel DG, Kaplan NL, Anderson MW: Implication of nonlinear kinetics on risk estimation in carcinogenesis. Science 1983; 219:1032-1037.

17. Griesemer TA, and Cueto C Jr: Toward a classification scheme for degrees of experimental evidence for the carcinogenicity of chemicals for animals. IN Molecular and Cellular Aspects of Carcinogen Screening Tests, R Montesano, H Bartsch, and L Tomatis (eds). International Agency for Research on Cancer, Lyon, France, 1980.

18. Crouch E, and Wilson R: Interspecies comparison of carcinogenic potency. J Tox Env Health 1979; 5:1095-1118.

19. Omenn GS: Genetics and epidemiology: medical interventions and public policy. Soc Bio 1979; 26:117-125.

20. Friedman RD: Sensitive Populations and Environmental Standards: A Legal Analysis. The Conservation Foundation, Washington, DC, 1979.

21. 44 Fed. Reg. 8215 (1979).

22. 43 Fed. Reg. 46252 (1978).

23. Omenn GS, Motulsky AG: Eco-genetics: genetic variation in susceptibility to environmental agents. IN Genetic Issues in Public Health and Medicine. BH Cohen, AM Lilienfeld, PC Huang (eds). CC Thomas, Springfield, Ill, 1978, pp. 83-111.

24. Omenn GS: Predictive identification of hypersusceptible individuals. J Occup Med 1982; 24:369-374.

25. Office of Technology Assessment, U.S. Congress: The Role of Genetic Testing in the Workplace. Washington DC 1983.

26. Koenig JQ, Pierson WE, Horike M, Frank R. A comparison of the pulmonary effects of 0.5 PPM versus 1.0 PPM sulfur dioxide plus sodium chloride droplets in asthmatic adolescents. J Toxicol Environ Health 1983; 11:129-139.

National Toxicology Program. Annual Plan for Fiscal Year 1982. Washington, DC: Government Printing Office, 249 p. (NTP-81-94).

27. Omenn GS, Brandt E, Rall DP, and others: Testimony on the National Toxicology Program. Investigations and Oversight Subcommittee, House Committee on Science & Technology, U.S. Congress, 15 July, 1981.

28. Lave LB, Omenn GS, Heffernan KD, Dranoff G: A model for selecting short-term tests of carcinogenicity. J Amer Coll Tox 1983; 2:125-130.

29. Weisburger JH, Williams GM. Carcinogen testing: current problems and new approaches. Science 1981 23 Oct; 214 (4519):401-407.

30. Needleman HL, Landrigan PJ: The health effects of low level exposure to lead. Ann Rev of Pub Health 1981; 2:277-298.

31. EPA: Air Quality Criteria for Lead. Washington, DC, December, 1977. EPA-600/8-77-017.

32. EPA: Proposed national ambient air quality standard for lead. Fed Reg 14 December, 1977; 42:63076-63094.

33. International Agency for Research on Cancer: Evaluation of the Carcinogenic Risks of Chemicals to Humans. IARC Monographs Supplement 1, Chemicals and Industrial Processes Associated with Cancer in Humans. IARC, Lyon, France, 1979.

34. National Toxicology Program (DHHS, PHS): NTP Technical Bulletin, issue #4, April, 1981.

35. Chemical and Engineering News: Production by U.S. chemical industry. 9 June, 1980, p. 35ff.

36. Cone MV, Baldauf MF, Martin FM, and Ensminger JT: Chemicals Identified in Human Biological Media: a Data Base. Second Annual Report, EPA 560/13-80-036A, ORNL/EIS 163/V2-81. EPA, Washington, DC, 1980.

37. Industrial Union Department, AFL-CIO v. American Petroleum Institute, 100 S. Ct. 2844, 66 L.Ed., 2nd 268 (1980).

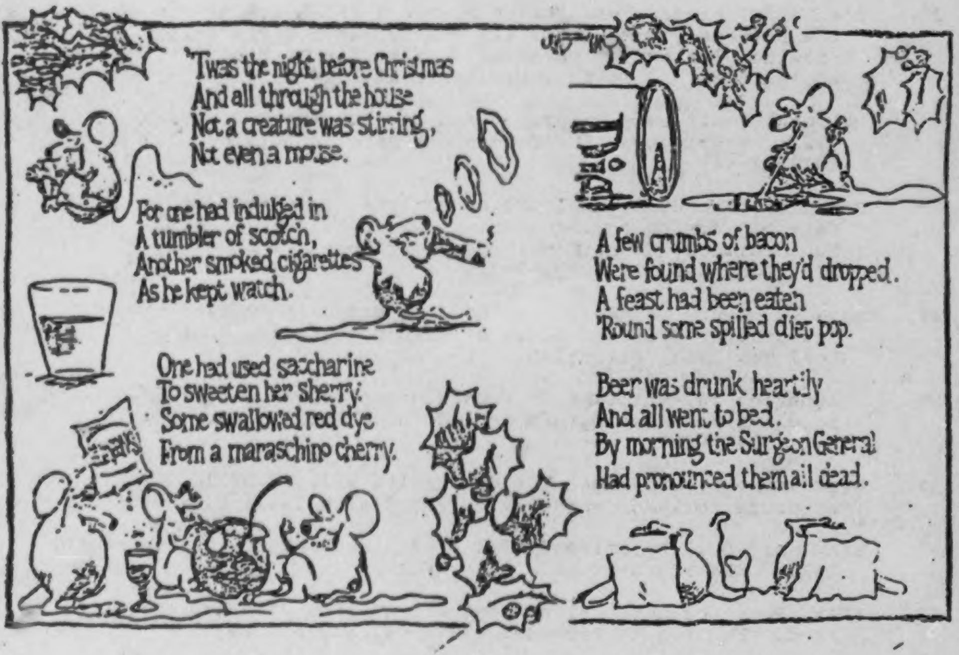
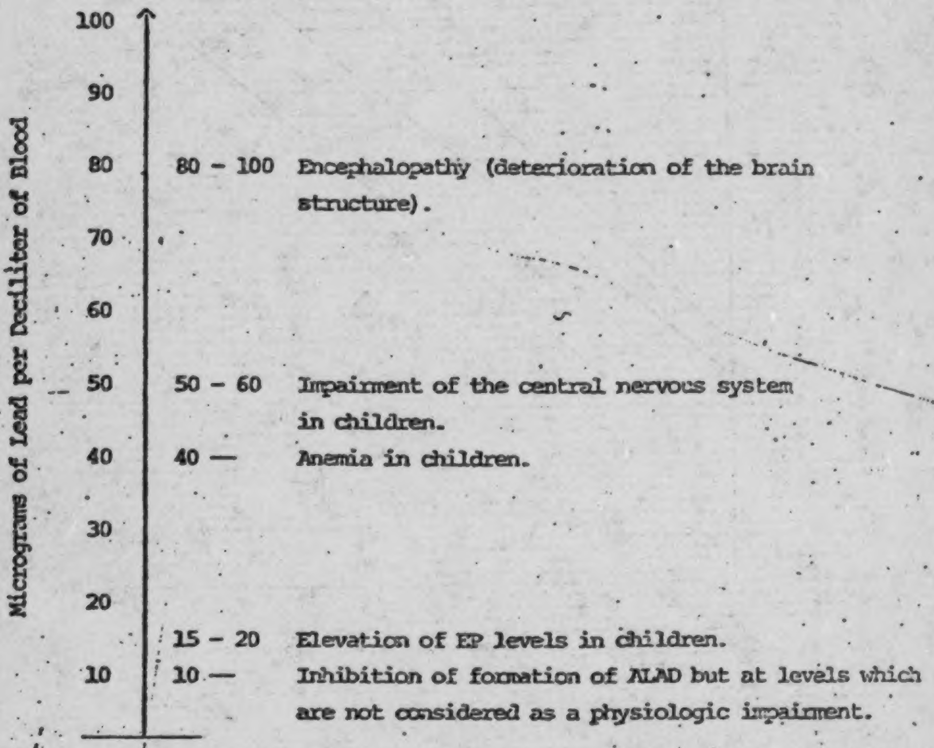

'Twas the night before Christmas
And all through the house
Not a creature was stirring,
Not even a mouse.
For one had indulged in
A tumbler of scotch,
Another smoked cigarettes
As he kept watch.
One had used saccharine
To sweeten her sherry.
Some swallowed red dye
From a maraschino cherry.
A few crumbs of bacon
Were found where they'd dropped.
A feast had been eaten
'Round some spilled diet pop.
Beer was drunk heartily
And all went to bed.
By morning the Surgeon General
Had pronounced them all dead.
Diet

Figure 1. Public perceptions of the ubiquitous environmental carcinogens. (From ref 7.)

Figure 2. BLOOD LEAD THRESHOLD FOR HEALTH EFFECTS



80 - 100 Encephalopathy (deterioration of the brain structure).

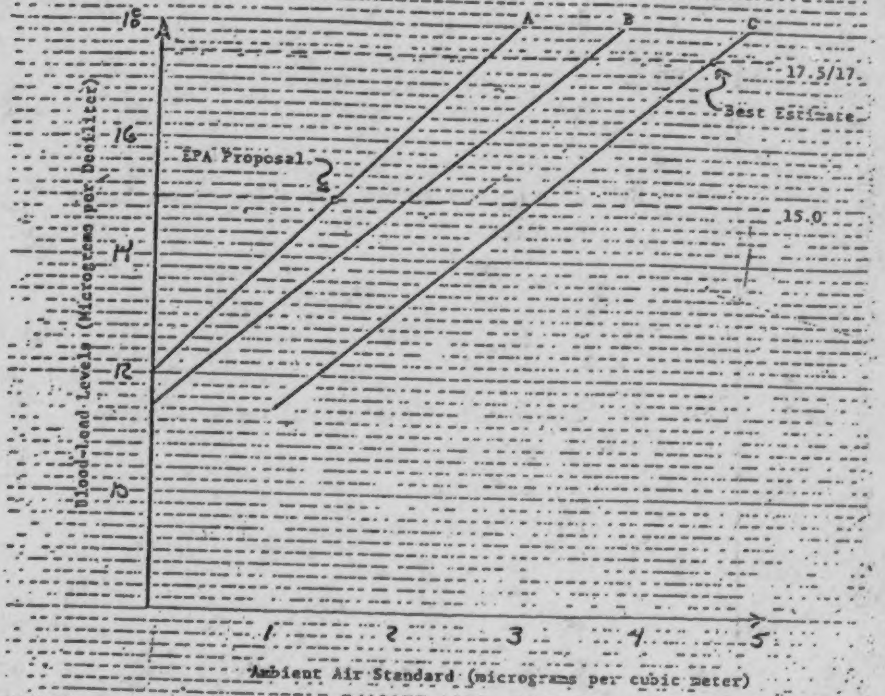
50 - 60 Impairment of the central nervous system in children.

40 — Anemia in children.

15 - 20 Elevation of EP levels in children.

10 — Inhibition of formation of ALAD but at levels which are not considered as a physiologic impairment.

* Based on figures in the EPA criteria document, "Air Quality Criteria for Lead."



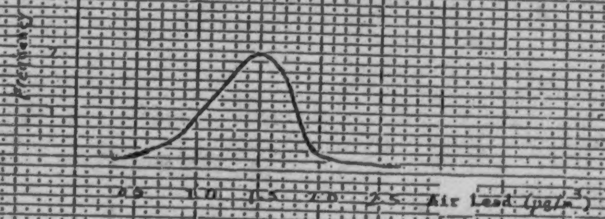
Alternative Assumptions:

A = EPA Assumptions.
B — "Best-Estimate"-Assumptions without Local Air-Lead Distribution Correctic
C = "Best Estimate" Assumptions with Local Air-Lead Distribution Correction.

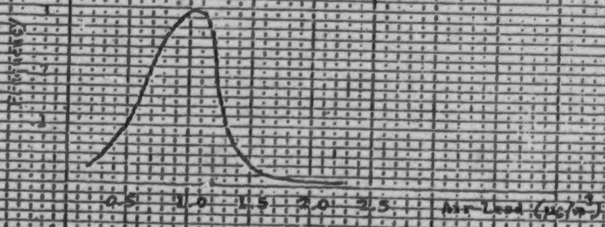
Alternative Blood-Lead Levels:

15.0 EPA Threshold for EP Elevation.
17.5 "Best-Estimate"-Threshold for EP Elevation.
17.7 Mean Level to Keep 99% of Critical Population Below a Blood-Lead Level of 40, the Level Associated with Anemia.

Figure 4. Hypothetical post-regulation air-lead distributions based on monitoring/enforcement strategies which treat the standard: (a) as a ceiling after normal dispersion, or (b) as a ceiling in areas of peak concentration. (Omenn GS & Golden J, unpublished).



a. Air-Lead Distribution Using 1.5 µg/m³ as a Ceiling After Normal Dispersion



b. Air Lead Distribution Using 1.5 µg/m³ as a ceiling in Areas of Peak Concentration.

50%

TABLE 1

POTENTIAL HUMAN CARCINOGENS

FRAMEWORK FOR DECISION-MAKING IN THE UNITED STATES

1. IDENTIFICATION
    - EPIDEMIOLOGY
    - ANIMAL TESTS
    - IN VITRO SCREENING
2. CHARACTERIZATION
    - RELATIVE POTENCY
    - EXPOSURES
    - RANGE OF SUSCEPTIBILITY
3. CONTROL
    - INFORMATION
    - REGULATION
    - SUBSTITUTION

TABLE 2

END-POINTS OTHER THAN CARCINOGENICITY

MUTATIONS

TERATOGENICITY: BIRTH DEFECTS

ALTERED REPRODUCTIVE FUNCTION

NEURO-BEHAVIORAL TOXICITY

OTHER SPECIFIC ORGAN SYSTEMS

GENETIC VARIATION IN HUMAN SUSCEPTIBILITY TO ENVIRONMENTAL AGENTS

DRUGS

Metabolism: N-Acetyl Transferase
Plasma Pseudocholinesterase
C-oxidation

Sensitivity: Glucose-6-phosphate dehydrogenase deficiency
Methemoglobin reductase deficiency

INHALED POLLUTANTS/PESTICIDES

Alpha-1 anti-trypsin deficiency
Aryl hydrocarbon hydroxylase inducibility
Metabolic conversion of nicotine
Plasma paraoxonase activity

FOODS

Lactose intolerance
Wheat gluten/celiac disease
Saturated fats/atherosclerosis
Fava beans
Goitrogens
Catecholamines

FOOD ADDITIVES and STIMULANTS

Iron Ethanol Caffeine

PHYSICAL AGENTS

Cold weather, motion sickness, metal poisoning, color vision, UV radiation, X-radiation

INFECTIOUS AGENTS/AUTOIMMUNE DISORDERS

Malaria: Duffy blood group; Sickle hemoglobin, thalassemia, G6PD deficiency
Predispositions due to impaired antibody production or cellular immunity
Predispositions associated with histocompatibility phenotypes

Table 4

REASONS CHILDREN ARE MORE SUSCEPTIBLE TO LEAD

1. Exposures/Intake
    - Hand to mouth: dusts, soils
    - Pica: Soil + Pb - paint
2. Ingestion/Absorption
    - 40% GI absorption vs. 10% in adults
    - Enhanced by Zn, Fe, Ca deficiency
3. Vulnerability of Developing Organs
    - Brain
    - Blood

Table 5

PERCENT OF CHILDREN WITH BLOOD LEAD 30 ug/dl.

(1976-1980 HANES DATA)

	All	White	Black
Males	4.3	2.1	13.5
Females	3.5	1.8	10.9
Both Sexes	3.9	2.0	12.2

Children 6 months to 5 years of age.
Estimated number nationally 675,000

NOTE: Among black children in central cities in families with annual income less than $6000 incidence of elevated blood lead levels was 18.6%.

Table 6

CALCULATION OF THE AIR STANDARD (1978)

EPA has calculated the standard based on the conclusions reached in the previous sections:

1. Sensitive population: children, ages 1 - 5.
2. Health basis (lowest detectable adverse effect): elevation of erythrocyte protoporphyrin (EP).
3. Effect threshold in sensitive population: 15 µg Pb/dl.
4. Assumed goal for contribution to blood lead from non-air sources: 12 µg Pb/dl.
5. Allowable contribution to blood lead from air sources: 15 µg Pb/dl - 12 µg Pb/dl = 3 µg Pb/dl.
6. Air lead concentration consistent with blood lead contribution from air sources:

$$3\ \mu g\ Pb/dl\ blood \times \frac{1\ \mu g/m^3\ air}{2\ \mu g/dl\ blood} = 1.5\ \mu g\ Pb/m^3$$

Table 7 lays out the range of evidence for the three crucial steps in the analysis, presents the EPA conclusion, and lists a mean value based on the available evidence. These data may be used to indicate the cumulative effect of EPA's fairly consistent use of evidence at the conservative end of the available range.

Table 7. The Range of Evidence, the EPA Estimate, and a Mean Estimate

	Range	EPA	Mean
1. Blood Lead Level at which Pivotal Health Effect Occurs:*			
a. Anemia			40.0
b. EP Elevation	15-20	15	17.5
2. Blood Lead Level Attributed to Non-Air Sources*	10-12.7**	12	11.3
3. Ratio of Blood Lead Level to Air Exposure in Children***	1.2-2.3	2	1.7

* Micrograms per Deciliter.

** The upper limit is the average obtained from four studies of children. The lower limit is from isotope studies.

*** Micrograms per Deciliter/Micrograms per Cubic Meter.

Table 8. - Proportion of a 10km radius area at different air-lead concentrations based on a hypothetical St. Louis lead smelter in compliance with a standard of 1.5 $\mu g/m^3$*

Air-lead Concentration ($\mu g/m^3$)		Proportion of Area (%)
1.5		.1
1.2		.2
.9		.7
.8		3.0
.7		5.0
.6		7.0
.5		9.0
.4		11.0
.3		13.0
.2		15.0
.1		36.0
Average .4	Total	100.0

* (on next page)

Table 9

SETTING PRIORITIES FOR CARCINOGEN REGULATION

1. Establish Carcinogenic Potential
2. Estimate Relative Potency

   --in standard bioassay per μg chemical
3. Check Current Production
4. Estimate and Characterize Exposures to Humans

   --nature, routes, time-course
5. Check Body Burdens: EPA Data Base
6. Rank Relative Risk/Priority for Risk Reduction

QUESTION: HAVE REGULATORY AGENCIES REGULATED THOSE CHEMICALS CONSIDERED HIGHEST RISKS?

Risk Assessment in the Federal Government: Managing the Process

Committee on the Institutional Means for
Assessment of Risks to Public Health

Commission on Life Sciences

National Research Council

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Summary

SETTING

This report explores the intricate relations between science and policy in a field that is the subject of much debate--the assessment of the risk of cancer and other adverse health effects associated with exposure of humans to toxic substances. It is a report of a search for the institutional mechanisms that best foster a constructive partnership between science and government, mechanisms to ensure that government regulation rests on the best available scientific knowledge and to preserve the integrity of scientific data and judgments in the unavoidable collision of the contending interests that accompany most important regulatory decisions.

Many decisions of federal agencies in regulating chronic health hazards have been bitterly controversial. The roots of the controversy lie in improvements in scientific and technologic capability to detect potentially hazardous chemicals, in changes in public expectations and concerns about health protection, and in the fact that the costs and benefits of regulatory policies fall unequally on different groups within American society.

The decade of the 1970s was a period of heightened public concern about the effects of technology on the environment. Individuals and groups urged strict government regulation as scientific evidence emerged that various chemical substances may induce cancers or other chronic health effects in humans, and new government programs were established to control potential hazards. The evidence of health effects of a few chemicals, such as asbestos, has been clear; in many more cases the evidence is meager and indirect. To aid decision-making, agencies have developed procedures for identifying chronic health hazards and estimating the risks to human health posed by products and activities. However, rather than alleviating the controversy attending regulatory decisions, the procedures themselves have become a focus of criticism by scientists, industry representatives, and public-interest groups.

STUDY OBJECTIVES AND SCOPE

The Committee on Institutional Means for Assessment of Risks to Public Health was formed, in response to a congressional directive, to fulfill three primary objectives:

- To assess the merits of separating the analytic functions of developing risk assessments from the regulatory functions of making policy decisions.
- To consider the feasibility of designating a single organization to do risk assessments for all regulatory agencies.
- To consider the feasibility of developing uniform risk assessment guidelines for use by all regulatory agencies.

The Committee considered the current practice of risk assessment and its relation to the process of regulation of hazards to human health, past efforts to develop and use risk assessment guidelines, the experience of government regulatory agencies with different administrative arrangements for risk assessment, and various proposals to modify risk assessment procedures. Our study was directed primarily, although not exclusively, to the issue of increased risk of cancer resulting from exposure to chemicals in the environment, an issue that has aroused great public concern in recent years, as illustrated by the controversies involving the control of saccharin, asbestos, and formaldehyde. Despite this emphasis, however, our conclusions and recommendations are applicable in some degree across the broad field of environmental health.

Criticisms of risk assessment have ranged broadly from details of the process to administrative management to statutory authority. The mandate to this Committee did not include examination of the scientific issues involved in risk assessment or the broad social policy questions that have been raised. The Committee's more limited purpose was to examine whether altered institutional arrangements or procedures can improve regulatory performance.

THE NATURE OF RISK ASSESSMENT

Regulatory actions are based on two distinct elements, risk assessment, the subject of this study, and risk management. Risk assessment is the use of the factual base to define the health effects of exposure of individuals or populations to hazardous materials and situations. Risk management is the process of weighing policy alternatives and selecting the most appropriate regulatory action, integrating the results of risk assessment with engineering data and with social, economic, and political concerns to reach a decision.

Risk assessments contain some or all of the following four steps:

- Hazard identification: The determination of whether a particular chemical is or is not causally linked to particular health effects.
- Dose-response assessment: The determination of the relation between the magnitude of exposure and the probability of occurrence of the health effects in question.
- Exposure assessment: The determination of the extent of human exposure before or after application of regulatory controls.
- Risk characterization: The description of the nature and often the magnitude of human risk, including attendant uncertainty.

In each step, a number of decision points (components) occur where risk to human health can only be inferred from the available evidence. Both scientific judgments and policy choices may be involved in selecting from among possible inferential bridges, and we have used the term risk assessment policy to differentiate those judgments and choices from the broader social and economic policy issues that are inherent in risk management decisions. At least some of the controversy surrounding regulatory actions has resulted from a blurring of the distinction between risk assessment policy and risk management policy.

UNIFORM GUIDELINES FOR RISK ASSESSMENT

An inference guideline is an explicit statement of a predetermined choice among alternative methods (inference options) that might be used to infer human risk from data that are not fully adequate or are not drawn directly from human experience. For example, a guideline might specify the mathematical model to be used to estimate the effects of exposure at low doses on the basis of the effects of exposure at high doses.

Over the last 2 decades, most federal regulatory agencies and other institutions responsible for risk assessment of toxic chemicals have sought to develop such guidelines. Their efforts have met with varied success. Agencies have cited several reasons for writing guidelines: to provide a systematic way to meet statutory requirements, to inform the public and regulated industries of agency policies, to stimulate public comment on those policies, to avoid arguing generic questions anew in each specific case, and to foster consistency and continuity of approach. Interagency guidelines for carcinogens, although short-lived, were developed by the agencies of the Interagency Regulatory Liaison Group (IRLG) and adopted by the President's Regulatory Council in 1979. The stated objective of that effort was to reduce inconsistency, duplication of effort, and lack of coordination among the federal agencies.

The form of guidelines varies widely. Some guidelines are comprehensive and detailed, addressing most of the components of risk assessment and describing underlying scientific concepts; others address only a few broad principles. Guidelines differ greatly in their degree of flexibility, i.e., the degree to which they permit assessors to consider scientific evidence that may justify departures from the prescribed inference options. And they vary in the legal authority vested in them: some are adopted as formal regulations and others by less formal means.

The Committee concludes that guidelines are feasible and, if properly designed, desirable; that clear statements of the inferences to be made in each step would be of advantage to the regulatory agencies, to the industries concerned, and to the general public; and that guidelines should be used uniformly by the governmental agencies.

INSTITUTIONAL ARRANGEMENTS FOR RISK ASSESSMENT

Dissatisfaction with government regulatory actions has led to proposals to restructure the institutional arrangements for risk assessment by:

- Organizational separation of risk assessment from risk management.
- Centralization of risk assessment activities in a single organization to serve all the regulatory agencies.

Four federal agencies--the Environmental Protection Agency (EPA), Food and Drug Administration (FDA), Occupational Safety and Health Administration (OSHA), and Consumer Product Safety Commission (CPSC)--have been given primary authority to regulate activities and substances that pose chronic health risks, and these four agencies' past actions have inspired many of the proposals for institutional change. The Committee reviewed a number of agency structures and procedures in an attempt to determine the merits of institutional separation and centralization. Examples were selected to illustrate different degrees of separation and centralization in the four agencies. Independent scientific review panels have been used to obtain some of the advantages proposed for organizational separation, and some of their experiences were examined.

Cross-agency comparisons are difficult, because the regulatory agencies and their various programs differ markedly in structure, procedures, personnel characteristics, administrative history, and statutory direction. In addition, agencies and programs change, and practices adhered to for several years may be altered substantially. These practical limitations to the evaluation of agency structures and practices led the Committee to conclude that predicting the likely effects of organizational rearrangements on agency performance of risk assessment is unavoidably judgmental. However, the available evidence shows no clear advantage of one administrative structure over another.

CONCLUSIONS AND MAJOR RECOMMENDATIONS

Dissatisfaction with the actions of federal regulatory agencies is often expressed as criticism of the conduct and administration of the risk assessment process. The

Committee believes that the basic problem in risk assessment is the sparseness and uncertainty of the scientific knowledge of the health hazards addressed, and this problem has no ready solution. The field has been developing rapidly, and the greatest improvements in risk assessment result from the acquisition of more and better data, which decreases the need to rely on inference and informed judgment to bridge gaps in knowledge.

Proposals to separate the administrative responsibility for risk assessment from risk management imply that the change would lead to improved risk assessment and hence better risk management decisions. Administrative relocation will not, however, improve the knowledge base, and, because risk assessment is only one element in the formulation of regulatory actions, even considerable improvements in risk assessment cannot be expected to eliminate controversy over those actions.

Organizational separation may have the advantage of establishing firmly the distinction between risk assessment and risk management, but it also has some disadvantages. The importance of distinguishing between risk assessment and risk management does not imply that they should be isolated from each other; in practice they interact, and communication in both directions is desirable and should not be disrupted. Institutional separation would surely reduce the responsiveness of the risk assessment process to the needs of the regulatory agencies for timely reports in accord with their priorities. In addition to the operational disadvantages, the disruption of current patterns of activity would be great, and the benefits uncertain. On balance, the Committee believes that transfer of risk assessment functions to an organization separate from the regulatory agencies is not appropriate.

We believe that risk assessment can be improved more surely and more effectively by adopting a program with three major parts: (A) implementation of procedural changes to ensure that individual assessments routinely take full advantage of the available scientific knowledge, while preserving the diversified approaches to the administration of risk assessment necessary to accommodate the varied needs of federal regulatory programs; (B) standardization of analytic procedures among federal programs through the development and use of uniform inference guidelines; and (C) creation of a mechanism that will ensure orderly and continuing review and modification of risk assessment procedures as the scientific knowledge base expands.

(A) We recommend that regulatory agencies take steps to establish and maintain a clear conceptual distinction between assessment of risks and consideration of risk management alternatives; that is, the scientific findings and policy judgments embodied in risk assessments should be explicitly distinguished from the political, economic, and technical considerations that influence the design and choice of regulatory strategies.

We agree with proponents of such measures as the American Industrial Health Council's proposed science panel and H.R. 638 that efforts should be made by regulators and others to distinguish clearly between the assessment of risk and the choice of regulatory options.

We advocate the adoption of specific procedural measures that can be introduced under current arrangements. These measures include timely independent scientific review of major agency risk assessments and, to facilitate both scientific and public review of risk assessments, the routine preparation of written risk assessments that explicitly state the basis of choice among inference options.

(B) We recommend that uniform inference guidelines be developed for the use of federal regulatory agencies in the risk assessment process.

The Committee endorses the development and use of guidelines for risk assessment. These guidelines, which would structure the interpretation of scientific and technical information relevant to the assessment of health risks, should be followed by all federal agencies. They should address all elements of risk assessment, but allow flexibility to consider unique scientific evidence in particular instances.

The use of uniform guidelines would promote clarity, completeness, and consistency in risk assessment; would clarify the relative roles of scientific and other factors in risk assessment policy; would help to ensure that assessments reflect the latest scientific understanding; and would enable regulated parties to anticipate government decisions. In addition, adherence to inference guidelines will aid in maintaining the distinction between risk assessment and risk management.

(C) We recommend to the Congress that a Board on Risk Assessment Methods be established to perform the following functions:

(1) To assess critically the evolving scientific basis of risk assessment and to make explicit the underlying assumptions and policy ramifications of the inference options in each component of the risk assessment process.

(2) To draft and periodically to revise recommended inference guidelines for risk assessment for adoption and use by federal regulatory agencies.

(3) To study agency experience with risk assessment and evaluate the usefulness of the guidelines.

(4) To identify research needs in the risk assessment field and in relevant underlying disciplines.

The Committee concludes that success in improving the risk assessment process requires the establishment of an independent board of scientific stature. Such a board can serve as a continuing locus of discussion about ways to improve scientific and procedural aspects of risk assessment.

Additional Questions:

Senator Hatch. During the hearings, reference was made to the risk of one in one million per lifetime (1×10^{-6}). Please explain what this means.

Mr. Omenn. This expression means that the risk of any specific adverse effect would be increased by one case per million people exposed. It is essential in understanding such a statement that the adverse effect, the exposure, and the people exposed be clarified.

Furthermore, the risk estimation process generally utilized presents what are called "upper risk estimates", technically the upper 95th confidence limit. For all practical purposes, this means that the risk "should not be higher than" the one in a million additional cases.

"One cancer in a million people exposed"requires information about the background incidence and the number of people so exposed. For example, with lung cancers, there are currently more than 120,000 new cases per year, with more than 105,000 deaths, in the U.S. Adding one more case in the whole country, or even one for every million adults in the country, would be impossible to detect against such a high background incidence. In contrast, when a peculiar kind of liver cancer occurred in a few workers with high exposures to vinyl chloride monomer, the connection was recognized because that kind of cancer was very rare in the general population. Likewise, if only a few thousand people are exposed to an agent, a risk of one per million people exposed would have to be evaluated in light of the extremely low probability that even one case would be found in such a small sample.

Senator Hatch. It is frequently said that quantitative risk assessment almost certainly overstates the actual risk because of the conservative assumptions used. Please describe these assumptions and why they are conservative.

Mr. Omenn. It is true that the quantitative risk estimates generally presented utilize conservative assumptions. The rationale is that it is "prudent" to "err on the side of protecting the public health". Much Congressional language supports such an approach, of course.

Such intent underlies the following practices:(1)the use of positive results, i.e. empirical studies showing adverse effects from a particular agent, even though other studies might have failed to find such effects; (2) the use of upper 95th confidence limits (as well as lower 95th confidence limits) to indicate the statistical uncertainty in the specific set of data and to be fairly confident that the actual incidence is not higher than the observed incidence, usually in a small number of animals or a small number of workers; (3) the use of the most sensitive species or strain of laboratory test animals, because of the marked variation in susceptibility among humans and the desire to be able to protect the most susceptible exposed people; (4) the linear extrapolation from observed dose-response ranges (corrected to the 95th confidence limit) to much lower dose levels of the sort the general population might face, or workers

Mr. Omenn (cont'd):

might still face even after extensive engineering controls; and (5) the use of increased tumor incidence in any organ, even when there is already a high background incidence in that organ or when there is no direct evidence for any comparable effect in humans, based upon the approach that animal tests are really intended to find carcinogenic potential of the compound, rather than the precise effects that might occur in humans.

The National Research Council Report goes into much more detail about these and many other specific "components" of the several steps of identification of a hazard, assessment of the dose-response relationship, assessment of the actual and potential exposures, and characterization of the risks to humans.

I hope that this brief summary is useful.

Senator **Grassley**. Thank you.

Dr. Stallones.

STATEMENT OF REUEL A. STALLONES, M.D., DEAN, SCHOOL OF PUBLIC HEALTH, UNIVERSITY OF TEXAS

Mr. **Stallones**. Thank you, Senator Grassley.

My name is Reuel Stallones. I am professor of epidemiology and dean of the School of Public Health of the University of Texas Health Science Center at Houston. I very much appreciate the opportunity to appear at this hearing. My comments will be brief and, again, a longer report has been submitted for the record should the committee choose.

I was chairman of the National Research Council Committee on Institutional Means for Risk Assessment. That committee was established to respond to a charge by the Congress of the United States to study the administrative processes involved in risk assessment in the regulatory agencies of the Federal Government—matters related to authority, responsibility, and control. We were asked to consider the desirability of centralizing the tasks of risk assessment and locating those procedures in an agency separate from the existing one, and further to consider the feasibility of developing and adopting guidelines for risk assessment. The report of the committee was issued in February of 1983.

Disease is imbedded in the environments of man. That is, all of human illness is, in greater or lesser degree, environmentally determined and hence preventable by appropriate environmental modification. In the past two decades attention has been focused sharply on control of hazards in the physical environment by governmental regulation. This is best illustrated by regulatory actions intended to reduce or eliminate exposure to carcinogenic chemicals employed or generated in the manufacture and marketing of food and other products for human use and consumption.

Regulation has been accompanied by swirls of controversy and litigation, as has occurred with respect to saccharin, benzine, asbestos, formaldehyde, and many other substances. The debates have involved both the evaluation and interpretation of the scientific information on hazards to health, that is, the risk assessment, and also the evaluation and selection of procedures to control the hazards, that is, risk management.

Risk management is governed by policy, policy compounded of social, economic, and political considerations separate and distinct from the scientific issues. Risk assessment is based on two kinds of information: direct epidemiologic data on human illness, and indirect information obtained from laboratory experiments with animals and in other systems.

Although epidemiologic observations are the strongest evidence of human health effects, adequate information is commonly lacking. To await the compilation of sufficient human experience is not acceptable, for this requires that people be subjected to an uncertain risk which might have, for them, catastrophic consequences. As an alternative, we are forced to rely on data obtained from experimentation of animals.

To infer human health effects from experience with animals requires extrapolation, and this extrapolation is usually performed in accord with some mathematical and biological models or concepts. Many models are available from which to choose, and the choice is sometimes arbitrary in the sense that no definitive biological principles exist to guide the selection.

In a formal risk assessment, different people may elect to proceed in different ways, using different models, leading to great variation in the estimates of risk, and this in turn may lead to very different actions by regulatory agencies. This inconsistency is disturbing and confusing, and promotes mistrust and litigation.

Although the primary problem—that the information base is inadequate—cannot be repaired by any administrative modification, our committee, the Committee on Risk Assessment, judged that the development and adoption of uniform inference guidelines would introduce much needed consistency and predictability into the risk assessment process. The guidelines should be formulated by an independent panel of distinguished scientists, and the guidelines should be subjected to review and revision as the science on which risk assessment is based advances.

The committee reviewed the activities of the major Federal regulatory agencies and found that although many differences exist among them, no particular mode of operation was clearly, significantly the best. The advantages of locating the reponsibility for risk assessment within those agencies are marked. This provides assurance that the conduct of risk assessment is timely and responsive to the missions of the agencies. The conduct of risk assessment within an agency promotes interaction between the science of assessment and the application of control procedures.

The total workload represented by the risk assessment activities of all the regulatory agencies is quite heavy, and to centralize this would require the creation of a large and, we think, unwieldy organization. The committee, therefore, concluded that separation and centralization of risk assessment for the Federal Government was not desirable.

However, the advantages of separation are important and they could be obtained by a functional separation of risk assessment from risk management within each of the regulatory agencies. This is quite feasible within the existing administrative structures.

Peer review of risk assessment performed by the staffs of the Federal regulatory agencies is a common practice, employing for that purpose advisory panels of scientists from outside the agencies. This provides many of the advantages expected from removal of responsibility for risk assessment from the agencies, and the committee recommended that the practice be adopted universally and, further, that external review be performed before risk management decisions are announced.

In summary, the Committee on Institutional Means for Risk Assessment has recommended: One, administrative responsibility for risk assessment for the Federal regulatory agencies continue to reside within those agencies but clearly separated from risk management; two, risk assessments prepared by the staffs of the Federal regulatory agencies be reviewed by independent panels of experts prior to announcement of regulatory actions; three, a special panel of scientists be established to develop uniform inference guidelines for risk assessment, reflecting the best scientific knowledge and judgment available, and, further, that the guidelines be reviewed and revised by that panel as needed; and, four, the guidelines be adopted by all of the Federal regulatory agencies to promote consistency and predictability in control activities.

Thank you, Senator.

[Responses of Dr. Stallones to questions asked by Senator Hatch follow:]

DR. STALLONES

ADDITIONAL QUESTIONS PREPARED BY SENATOR HATCH

1) During the hearings, reference was made to the risk of one in one million per lifetime (1×10^{-6}). Please explain what this means.

2) It is frequently said that quantitative risk assessment almost certainly overstates the actual risk because of the conservative assumptions used. Please describe these assumptions and why they are conservative.

Query #1: Please explain what is meant by a risk of one in one million per lifetime.

Response: The risk of disease may be expressed in many ways, such as the number of cases per 1,000 population per year. In quantitative risk assessment, the risk of an event, such as a stated form of cancer, is commonly given as a lifetime risk; that is, based on the information available from epidemiological data or animal experimentation, an estimate is derived of the probability of the occurrence of the event during the course of one persons lifetime in the presence of a defined intensity of exposure. Therefore a risk of one in a million per lifetime means that a defined exposure to a hazardous substance is expected to produce one case of the disease during the lifetimes of one million persons suffering that exposure.

Query #2: How does quantitative risk assessment lead to an overstatement of the actual risk by invoking conservative assumptions?

Response: In the course of risk assessment, inferences are necessary to bridge the gaps that exist between direct observations of human experience. Often an extrapolation is necessary to estimate the effects of exposure at doses lower than those employed in animal experimentation; if a mathematical model is used for this extrapolation which is based on the principle that no threshold exists for the risk associated with exposure to that substance, the estimate of risk at the low dose will be much higher than if a different (threshold) model were used. In carrying forward an estimate of risk from either animal experiments or epidemiological observations, a conservative assumption will dictate the use of the upper 95% confidence limit of the observation rather than the observed value, leading to an overstatement of the risk. Many other assumptions may have a similar effect, such as a decision to use a count of all tumors (including those commonly considered to be benign) induced in experimental animals as the basis for estimating the risk of cancer in humans; the decision to use the experimental data from that experiment which yielded the highest number of tumors, rather than an average of all experiments; or the decision to rely on epidemiological data which showed positive results, while ignoring negative studies. The argument for adopting these assumptions is that a regulatory agency has a responsibility to err on the side of conservatism in protecting the public's health, and the most conservative approach is overstate the risk so that the regulatory action will require more stringent control of hazardous substances than would otherwise be the case.

Senator **Grassley**. Thank you. I have several questions, and they aren't directed at any one specific person so I would like to have one person jump in, and then to the extent which the other two have anything to add. I would appreciate it very much.

Just to reinforce my understanding, a risk of 1 in 1 million does not mean that 1 in 1 million persons will actually die. Is that correct?

Dr. **Rodericks**. Ordinarily—if you are talking, Senator, about the way risk assessment is now practiced— no, it does not mean that. The number itself, which is one of the products of a risk assessment, should I think never be interpreted in isolation from the methods and assumptions used to arrive at the number. The number in fact can mean quite different things for different agents.

I suppose in an extreme case where all the assumptions accorded directly with reality—and I have never seen a case like that—it would mean strictly speaking that if every member of a population of, let's say, 1 million people, if every member of that population were exposed to a given level to cause that risk from birth to death, that one of those people might develop cancer over a 70-year period, about a lifetime. However, that would be unusual. I have never seen an assessment where the assumptions would accord with reality in that way.

We cannot, however, quantify the difference between the number we predict and the actual number, which as far as I can tell is always likely to be very, very much lower. Therefore, no, it would be incorrect ordinarily to assume that it means a death in a population of 1 million.

Senator **Grassley**. Well, is the setting of a quantitive risk level at, we will say, 1 in 1 million, really equivalent to insuring that the risks are so low that there are no public health consequences?

Mr. **Omenn**. Yes. I think that is the reason that the FDA has chosen that value, in order to present to the public the results of an analysis which they believe to be consistent with assurance that the risk below that level would be insignificant.

Senator **Grassley**. Let me clarify another point. I think none of you, if I am correct, is saying that the regulatory decision should be made by utilizing quantitative risk assessment exclusively. Is that correct?

Mr. **Omenn**. More than that, we say that a formulation which proposes that a decision should be made on a risk assessment alone fails to understand the process. First of all, there must be data and the data must be analyzed for their appropriateness and strength of evidence.

Then there must be the risk assessment, and we believe that risk assessment should be done by people different from the people who make the regulatory decision. Then we believe that the quantitative and especially the qualitative information from the risk assessment should be utilized, together with a host of other information, to make a regulatory decision.

Senator **Grassley**. Therefore, then, the point I was trying to make is that the risk assessment should be just one part of the regulatory decisionmaking process.

This is a more general question, and maybe one that would let you roam all over the ball park, but to the extent to which you could zero in it would be very helpful to us: What guidance should the Congress give an agency, in this particular case the Food and Drug Administration, in setting the appropriate level of risk?

Dr. **RODERICKS**. May I respond first, Senator?

Senator **GRASSLEY**. Sure.

Dr. **RODERICKS**. I don't think the Congress should specify a number because, as I said, too much depends on the qualitative aspects of the risk assessment. The number means different things for different compounds, where you have different kinds of evidence. For a compound that may have a threshold, the number may mean quite something different than for an initiator, for example, and that sort of information needs to be taken into account when making the decision.

I think the best guidance that Congress might give is for the agency, No. 1, to define in a general way what insignificant risk means, and then in specific cases be asked to show in quite explicit ways how the risk assessment was used, what sort of evaluation then followed that to reach the decision that a risk was insignificant or significant in a particular case, and then subject that to some kind of public review. It is not just a subjective judgment, but I think there is an analytic process that the agency should be obliged to go through.

Mr. **OMENN**. Senator, I think there are two kinds of things Congress can and should do in this area. The first has to do with the process, and there are specific recommendations in the report of the panel which Dr. Stallones chaired and described which I think would be appropriately addressed by this committee, as well as by other committees of the Congress.

We recommended that there should be a panel set up at the request of the Congress to look at the appropriate guidelines for the doing of risk assessments, making inferences from available data so that the risk assessments would be comparable across agencies or even within agencies for different exposure situations. We believe that consistency and comparability, the capacity to generate relative risk that means something, is essential to the proper use of risk assessment in regulatory decisionmaking. I believe it falls to the Congress to order such a panel and to provide some funds for its functioning.

Beyond that, the process could be greatly enhanced if the Congress, through the various committees which have jurisdiction over the respective agencies—and, specifically, this committee, with the FDA—would instruct those agencies to review the recommendations from such an outside panel and enter a process to adopt those recommendations or revisions of those recommendations jointly, so that across FDA, EPA, OSHA, and the Consumer Products Safety Commission there would be common rules for how to approach the data, including rules for how to introduce new scientific information as it becomes available. All that is spelled out in the report.

However, for these steps to be taken, positive action from Congress and from this committee, among others, will be essential.

The second role for the Congress, I believe, is to review the values that agencies are currently utilizing in determining insignificant risk. It is quite interesting, as a matter of fact—although the numbers are close enough that you could say they really are not distinguishable—that FDA uses a value of 1 in 1 million, 10 to the −6. EPA has used a value of 10 to the −5, 10 times higher. With all the assumptions and the worst case scenerios, these differences should not be overestimated, but they do reflect a philosophy and a judgment that in the case of the food supply, a much larger population tends to be exposed than in the case of people around smelters or people in urban areas facing air pollution, or other even quite widely experienced hazards which EPA regulates. Congress could inquire in some detail from people in the agencies how useful these guidelines have been, which kinds of hazards have been excluded, and which have been pushed into the regulatory pipeline as a result of such 10 to the −6 or 10 to the −5 marks for insignificance of risk.

Another area which would warrant considerable attention from the Congress and was emphasized in my testimony is the definition of benefits to be considered by the agencies. As you know, there has been considerable interest from the present administration in cost-benefit analysis, although as far as I am aware there has been hardly any utilization of such techniques. I don't believe they are applicable in any practical way at present in these areas, but, in any case, there has not been much regulation, to my knowledge, which has employed them.

Our testimony today dealt only with health risk and health benefit tradeoffs I believe that here there is fertile ground for the Congress to stimulate some analysis. Even here it would be useful to know if the Congress feels, following the nitrites example, that the health benefit should be a major one like life-saving protection against botulism, or should it simply be increased shelf-life of food, or should it be enhancing the quality and reducing the costs of the food supply for general consumer benefit and better nutrition. Those are questions which really do require guidance from the Congress.

Senator GRASSLEY. Dr. Stallones.

Mr. STALLONES. Senator, the issue of establishing some stated acceptable risk in some quantitative terms is most interesting and probably an insoluble problem at the present time in this field. As Dr. Rodericks indicated—he didn't quite say it—but the number, the risk statement that emerges from quantitative risk assessment following extrapolation of at least two orders is an imaginary number, and its relation to a real number is not known. Therefore, if an explicit risk limit is established, either by an agency or by the Congress or in some other fashion, the risk estimate that derives from a quantitative risk assessment may comply or fail to comply with that regulated number according to some assumptions that are inserted into the risk assessment process.

Now I simply bring this up to illustrate how soft that number is. Whether a risk of 1 in 1 million of something or other is acceptable or not depends on a lot of things. As Dr. Omenn commented, the breadth of exposure within the population is a very important feature in what is an acceptable quantitative statement of risk. If everyone is exposed, if people are exposed in infancy, if people are exposed only while driving to work or only in the workplace, these matters all relate to how serious a problem is and what kind of risk I think might be tolerated.

In epidemiology we have difficulty measuring things at about a risk of 1 in 1 million. We can do this if the event is distinctive. For example, over about a 15-year period we had no smallpox in the United States but we had a lot of smallpox vaccination, and that vaccination for small children receiving their first immunization carried a price of one death for about every million vaccinations. We could measure that; that is how we know that it was 1 in 1 million. That is a hard estimate of the kind that Dr. Rodericks mentioned earlier, like counting people dead on the highway, not a soft estimate from an extrapolation.

Now whether that vaccination program conferred sufficient benefits on the people of the United States to warrant paying a price of one dead child per million vaccinations became a matter of considerable debate, and the debate was resolved and decided it was not worth it because the risk of naturally occurring smallpox approached zero. Therefore, there was effectively no benefit but still a cost.

I think much of that applies. Although the field is different and the analogy might not be as strong as one would like, many of the arguments apply when we move over into other aspects of environmental contaminants and pollutants and food safety.

Thank you, sir.

Senator GRASSLEY. Thank you.

I will close the panel with one observation on Dr. Rodericks' statement that current risk assessment overstates the magnitude of human risk, and you said sometimes substantially. I believe that when it comes to food safety policy this is an interesting and telling point, because what we then have is risk assessors who conduct studies which overstate actual human risk. Then in turn we have the risk managers, which would be another term for our regulators, apply rigid, inflexible regulations based upon the present rule of no risk. Then what we have is administration by overreaction to an overstatement, and this isn't very conducive to a useful food safety policy.

Of course, that is what this series of 3 days of hearings is all about, to hopefully establish a useful food safety policy not only for the consumer but for the producer and processor as well, not only for health but also for the good of the total society.

Thank you all very much for your participation. This meeting is adjourned, and will continue tomorrow on schedule. Thank you.

[Whereupon, at 12:15 p.m., the committee recessed, to reconvene at 9:30 a.m. on Friday, June 10, 1983, in room 430, Dirksen Senate Office Building.]

OVERSIGHT OF FOOD SAFETY, 1983

FRIDAY, JUNE 10, 1983

U.S. SENATE,
COMMITTEE ON LABOR AND HUMAN RESOURCES,
Washington, D.C.

The committee met, pursuant to recess, at 9:38 a.m., in room SD-430, Dirksen Senate Office Building, Senator Orrin Hatch (chairman of the committee) presiding.

Present: Senators Hatch, Quayle, and Grassley.

OPENING STATEMENT OF SENATOR HATCH

The CHAIRMAN. Today is the third day of the Labor and Human Resources Committee's hearings on food safety issues. When Senator Kennedy and I announced these hearings in a joint press release, we stated: "The hearings will focus on two central issues: No. 1, how recent scientific and technological developments have affected food safety regulation, and No. 2, whether existing law should be revised in order to accommodate advances in science and technology."

During the last 2 days we have heard from 12 distinguished scientists, 2 of whom, Dr. Donald Kennedy and Dr. Jere Goyan, were Commissioners of the Food and Drug Administration during the Carter administration. I might add that their testimony was excellent, and, I personally believe, irrefutable. From these 12 witnesses, we have heard a large number of varied views and observations about the two central issues and the law generally.

As I stated in my opening statement yesterday, I was struck by the extent to which Dr. Kennedy and Dr. Goyan, speaking from their particular experiences, agreed on a number of points, including:

No. 1, the food safety laws have generally worked well to protect the American public;

No. 2, scientific knowledge has advanced greatly since the food safety laws were last revised in 1958, and these advances have made parts of the law outmoded; and

No. 3, FDA is hampered in its ability to utilize its best scientific judgment in evaluating and in determining policy for various substances.

I have been interested in hearing to what extent our other distinguished witnesses have agreed or disagreed, both generally and specifically, with Dr. Kennedy's and Dr. Goyan's views. In this regard, the views of the other scientists we have heard have been most interesting.

I hope today's witnesses will prove as helpful in elucidating for the committee an answer to our central issues: No. 1, how recent scientific and technological developments have affected food safety regulation, and No. 2, whether existing law should be revised in order to accommodate advances in science and technology.

We have heard former FDA Commissioners and many fine scientists testify on a range of issues pertaining to food safety. Today we will approach the issue from a slightly different perspective as we hear from representatives of the administration's working group on food safety, representatives of consumer groups, and, finally, from representatives of industry groups.

Mr. C. W. McMillan, Assistant Secretary for Marketing and Inspection at the U.S. Department of Agriculture, will start us off this morning by presenting the findings of the working group. He is accompanied by Dr. Edward Brandt, Assistant Secretary for Health at the U.S. Department of Health and Human Services; Dr. Arthur H. Hayes, Commissioner of the Food and Drug Administration; and Dr. Donald L. Houston, Administrator of Food Safety and Inspection Service at the U.S. Department of Agriculture.

These gentlemen will take part in the question-and-answer period to follow Mr. McMillan's presentation.

Mr. McMillan, will you please begin?

STATEMENT OF C. W. McMILLAN, ASSISTANT SECRETARY FOR MARKETING AND INSPECTION SERVICES, DEPARTMENT OF AGRICULTURE, ACCOMPANIED BY EDWARD N. BRANDT, JR., ASSISTANT SECRETARY FOR HEALTH, DEPARTMENT OF HEALTH AND HUMAN SERVICES; ARTHUR H. HAYES, JR., COMMISSIONER, FOOD AND DRUG ADMINISTRATION, DEPARTMENT OF HEALTH AND HUMAN SERVICES; AND DONALD L. HOUSTON, ADMINISTRATOR, FOOD SAFETY AND INSPECTION SERVICE, DEPARTMENT OF AGRICULTURE

Mr. McMILLAN. Thank you very much, Mr. Chairman.

On behalf of my colleagues and me, we thank you for this opportunity to appear before you today and present the various findings that we looked at as the working group on food safety.

I will not introduce my colleagues again inasmuch as you already have done so, but we all are pleased to be here today.

First, I would like to ask Commissioner Hayes to outline for you certain dilemmas that we in the regulatory agencies face in dealing with this most complex and vexing issue of food safety.

Dr. Hayes, please.

Dr. HAYES. Thank you very much, and good morning, Mr. Chairman.

I am very pleased to be here today. Indeed, it is a privilege to participate in a discussion of food safety laws with such a distinguished panel.

These hearings are important—in fact, essential—in our assessment of the intricate relationship between science and the laws governing the safety of our Nation's food supply. It is an area that is fraught with controversy—controversy that has arisen from scientific advances in our ability to detect potentially hazardous chemicals.

Over the last 2 years and 2 months that I have been Commissioner of Food and Drugs, I have stated over and over again my underlying philosophy concerning any revisions in our food safety laws and that is—the public health is and should remain the focus of the food safety laws. This principle grows out of our understanding that the food safety laws are designed to protect and promote the public health and that any changes we develop must recognize and advance this important principle.

Sound regulatory decisions must be based on fundamentally good science, and if that were the entire story, all would be well. But, as you all know, we face a further dilemma: science is never complete; it is always evolving and rarely conclusive. Science, indeed, is dynamic. Its frontiers are growing and expanding constantly.

Twenty-five years ago when Congress gave the Food and Drug Administration additional regulatory authority over food additives, our science in many ways was relatively crude. In the 1950's good science was chemical residue detection in the one millionth range, but today good science means the ability to detect and quantify residues in the picogram range. This is one trillionth of a gram.

As these testing methods have become more sensitive and reliable they, along with other factors, have actually made the decisionmaking process much more complex than ever before because:

Detection levels for routine types of analyses have been lowered by three orders of magnitude.

Ten times as many chemicals are being tested today as were tested back in 1958, which in turn results in more carcinogenic constituents being found, that is, substances that are carcinogenic in animals, by the route of ingestion.

Many more parameters and considerations are being examined in toxicological investigations—the operation of metabolism, pharmacokinetics, absorption, and the utilization of new testing methodologies, like the in vitro mutagenic tests.

We are applying more sensitive methods of statistical analysis than ever before. In addition, other toxic phenomena, such as teratogenesis and mutagenesis, continue to concern us. Equally significant are the changes in how food is processed and consumed: There is a greater reliance on processed foods. Genetic engineering and better breeding techniques offer the potential for altering the nature of our food supply. There is a growing concern about the relationship between the diet and health. The potential exists for dramatically altering the nutritional components of our diet.

It is clear that our ability to make balanced regulatory judgments is being stretched to the limits. Although it made sense in 1958, when scientific methodology was less sophisticated, to limit scientific inquiry into the safety of food additives found to be carcinogenic in animal feeding studies, this approach has led to more and more problems as scientific methodology has advanced. The advances in analytical methodology described above have made it possible to detect at minute levels certain ubiquitous substances that may present a risk of cancer—albeit an insignificant risk. In many cases the Delaney clause does not permit what today is considered to be the exercise of sound scientific judgment in dealing with such insignificant risks.

The presence of very small amounts of carcinogenic constituents in color additives and packaging materials presents similar regulatory problems. The consideration of carcinogenic constituents in colors and indirect additives has become so frequent that, for all practical purposes, it is now a routine part of the petition review process.

Carcinogenic constituents have presented a problem in the regulation of color additives such as D&C Green No. 5, D&C Reds No. 6 and 7, and D&C Green No. 6. With indirect additives, such as packaging materials, carcinogenic constituents are sometimes present as byproducts of polymeric reactions, as impurities in reactants, and as the unreacted monomers of the final polymers.

The regulation of vinyl chloride provides an example of the difficulty in regulating packaging materials in which the monomer is a carcinogen. The issue of how to regulate vinyl chloride in packaging material has been under consideration since 1973. Analytical methods of everincreasing sensitivity have brought about the discovery of small amounts of this monomer in foods and prompted proposals to prohibit vinyl chloride for a wide variety of food packaging uses.

While administrative interpretation of the current food additives law has provided a means of addressing certain problems created by small amounts of carcinogenic impurities, it may not offer a complete solution. For example, the agency is confronted with the problem of functional food additives that are weak carcinogens, but that are present in such small quantities that they may not present a significant risk. An example of such an additive is the flavor, cinnamyl anthranilate. FDA has proposed a ban of this carcinogenic flavoring ingredient without any examination of its possible safety at very low levels of exposure.

Another problem presented by the current law is that it may soon be possible to conclude that a substance that is a carcinogen in animal species may not—because of anatomical, metabolic, or other factors—present a risk to humans. These scientific factors are excluded from the decisionmaking process under the Delaney clause.

One might argue that so long as there is no imminent threat to the nutritional adequacy of the food supply due to application of the current statutory scheme, a revision of our food safety laws is not necessary. I believe this view is very shortsighted. I cannot predict with certainty the advances in science that will take place in the next decade, but based on our experience since the enactment of the Delaney clause, I can only conclude that future problems concerning its application will be more significant than those we presently face.

Mr. Chairman, my comments have been drawn from my encounters with advancing science and the Federal Food, Drug, and Cosmetic Act during my tenure as Commissioner. They are not hypothetical; they are real. I hope these hearings will provide a better understanding of where science is, where it is going, and how advances in science pose real dilemmas for those responsible for assuring the safety of our food supply.

I believe these comments reflect much of what the committee heard from the scientists in the last 2 days and provide appropriate background for Mr. McMillan's statement.

The Chairman. Thank you, Dr. Hayes.

Mr. McMillan.

Mr. McMillan. Thank you, Mr. Chairman.

In the way of background, interest in revising the current food safety laws administered by the FDA and the USDA has been going on for some time. The events of the last few years have heightened the desire on the part of the public, the scientific community, Government, and industry to make changes in these laws. The nitrite situation made it clear that the law should be sufficiently flexible to deal with substances that may be questionable, but which may, nevertheless, provide important health benefits to consumers. Many commenters, both inside and outside the Government, now believe that we are finding ourselves increasingly constrained by food safety laws which have become scientifically outdated.

There are serious questions that cannot be addressed within the framework of the current food laws—questions about the level of risk that is acceptable, the way that risk should be assessed and managed, and the possible tradeoffs between risks and benefits. Technology now enables us to detect infinitesimal levels of carcinogenic substances in food, thus compelling a more sensible way of reacting to these findings by Government and other interested parties.

We must keep in mind that any reevaluation of the existing food safety laws must begin with the recognition that we in the United States enjoy the most abundant and safe supply of food that the world has ever known. Our food cannot be rivaled for its safety, wholesomeness, variety, and availability. One major reason for this has been the basic soundness of the provisions of our food safety laws, which are administered by FDA and USDA.

However, inasmuch as the last major changes in our food safety laws occurred in the 1950's and 1960's, with the passage of the Food Additives Amendment of 1958, the Color Additive Amendments of 1960, the Drug Amendments of 1962 which related to animal drug residues in food for human consumption, and the Wholesome Meat Act of 1967, we believe that it is appropriate to examine whether modernization of the food safety laws is in order.

We have sought from the outset to develop our thinking on food safety issues in an open and constructive environment. We have released materials outlining our latest thoughts on the subject on two different occasions so that the public could help us identify problems and find reasonable solutions to them.

We have received comments from industry, consumers, scientists, Members of Congress and their staffs, and other interested groups and individuals. We have analyzed these comments thoroughly and have had followup meetings with many of the commenters.

The most significant food safety issues include:

One, whether to add a definition of the term "safe" to the Federal Food, Drug and Cosmetic Act;

Second, whether to change the FDC Act's Delaney clause from an essentially "zero risk" concept;

Third, whether to provide for the utilization of risk-benefit assessments in determining whether to prohibit the use of food ingredients;

Fourth, whether to use independent scientific review processes in making food safety decisions; and

Fifth, whether to authorize gradual phaseouts rather than immediate prohibition of substances that do not meet the safety standard.

A brief summary of our latest thinking on each of these issues follows:

"Safe" is defined in the legislative history of the Food Additives Amendment of 1958 as a "reasonable certainty of no harm under intended conditions of use." Many believe that the FDA has focused unduly on the reference to "no harm" in its interpretation of "safe" and that there has been an increasing tendency to insist on an absolute zero risk standard of safety for all food substances. Much of this concern may be attributed to the Delaney clause. There is also concern that, even if there were no Delaney clause, FDA, nevertheless, would apply a no-risk standard and insist on absolute safety.

Therefore, it is appropriate to consider including in the FDC Act a definition of "safe" clearly stating that a zero risk standard is not to be applied. Adding such a statutory definition could clarify the principles under which FDA operates and could minimize arbitrary drift from the announced safety standard.

With respect to the Delaney clause, the current law contains three separate anticancer clauses that are collectively referred to as a Delaney clause. Two of these provisions prohibit the FDA from approving food additives and color additives that induce cancer in man or animals. The third requires elimination of carcinogenic drugs from the edible tissues of meat animals and poultry prior to slaughter.

The principal argument against the Delaney clause is its inflexibility, as the clause has traditionally been interpreted. It does not permit factors such as the extent of human exposure to a substance, or the appropriateness of extrapolation of the test data from animals to man, to be considered in the safety assessment of a carcinogenic food additive, color additive, or new animal drug. It makes no allowance for the possibility of threshold doses for some carcinogens.

In essence, the Delaney clause short circuits indepth, scientifically sound consideration of the safety of a carcinogenic food additive, color additive, or new animal drug. In recent years the Delaney clause has created increasing problems because scientific and technical advances have uncovered in the human diet more and more substances in miniscule amounts that have been determined to be animal carcinogens. Although some administrative interpretations may make it possible to deal with some of these problems in the near term, clear legislative guidance is obviously preferable to the uncertainties of testing such interpretations in court.

Serious thought should be given to modifying the Delaney clause so as to allow FDA to use risk assessment to reach sensible results consistent with the public health. Such a statutory scheme would permit FDA to use the best science available to ascertain what the real risks presented by a substance are—that is, risk assessment—and then determine how best to manage that risk. Such a statutory scheme implies a recognition that certain foods do present risks, but that there is no need for restricting or banning such a food where the magnitude of the risk can be quantified and is considered insignificant.

With respect to the risk-benefit assessment, except for pesticides and, to a limited extent, environmental contaminants, the FDC Act does not provide for a balancing of benefits against risks for individual substances in food.

In issuing a food additive regulation or revoking a regulation for an additive which has a substantial history of use and for which there is no reasonably practicable substitute, the Secretary of HHS would be capable of making better decisions if she had authority to consider whether the risks to human health are acceptable on account of the benefits offered by the use of such an additive.

Scientific review is very important. Regulatory food safety decisions are frequently made under conditions of some degree of uncertainty. In the absence of institutionalized oversight, this situation often gives rise to doubts about the soundness, objectivity, and consistency of scientific decisions. Some people outside the Government believe that scientific decisions, especially on suspect carcinogens, are made without an adequate review of the underlying scientific or test data. To correct this perception, it would be useful for HHS and USDA to establish independent Food Safety Committees to conduct reviews of significant scientific findings pertaining to food safety issues.

Finally, phaseout authority: FDA's and USDA's laws contain no provisions for gradually implementing bans of food substances. This precludes any consideration of the consequences of abruptly removing a substance from the food supply and prohibits opportunities to provide for the safe and orderly removal of a product from the market.

FDA and USDA should have authority to gradually phaseout a substance. In determining whether to permit a phaseout, the Secretaries of HHS and USDA should be required to consider the history of use of the substance, availability of reasonably practicable substitutes, the risks associated with continued use of the substance, effects of such use on the nutritional value or availability of food, and whether an immediate ban would significantly disrupt the food supply or cause significant economic hardship.

This brief overview represents the latest collective thinking of those at this table with respect to some of the more important issues that should be addressed in any consideration of changes in our food safety statutes. It is important to note these views have neither been accepted nor rejected as official administration policy to date. Therefore, they should not be viewed as the ultimate and definitive statement of the administration's position on modifications of the foods safety laws. Rather, they should be looked upon as the latest development in a continuing search for needed improvements in our food safety statutes.

Let me end by making one final point. The administration is prepared to work with the Congress, the scientific community, consumers, and industry in formulating reasoned solutions to food safety issues. We recognize that finding such answers is not an easy task, and that there may be considerable and sometimes fractious debate over the appropriate course of action. But there will be no better time to undertake this labor than now.

Our hope is that all interested parties will approach this responsibility in a spirit of cooperation and commit themselves to the pursuit of scientifically sound regulatory decisionmaking, recognizing, of course, the limits of even the most advanced scientific techniques.

Surely there is no more fundamental concern to the people of this country than the safety of their food supply. Thus, the public health and well-being must remain the central focus of our endeavors. I, personally, look forward, as do all of my colleagues here at the table, to a continuation of our joint efforts to reach the commendable goal of modernizing our food safety laws so they reflect the most advanced scientific methods and concepts.

Mr. Chairman, this concludes my formal statement. We will be pleased to try to answer any questions that you and other members of the committee may have.

The CHAIRMAN. Thank you, Mr. McMillan, for your excellent statement, and yours, also, Dr. Hayes.

Let's focus on the safety standard. What observations led you to conclude that the definition of safe needs to be changed? What, in your opinion, would be an appropriate definition of "safe?"

Mr. MCMILLAN. Mr. Chairman, I would like for Commissioner Hayes to respond to that question, please.

The CHAIRMAN. Dr. Hayes?

Dr. HAYES. Mr. Chairman, ever since the current food additive laws were passed in 1958, 1960, and 1962 in the case of animal drugs in the human food supply, there has been a recognition—indeed, a growing recognition—that the goal with respect to the safety of the food supply is just that—that the foods that are available are safe.

There has also been a growing recognition that it is not possible for safe to mean that there is a zero risk. On the one hand, as Commissioner Kennedy discussed the other day, the language of the current safety standard is confusing.

In 1958, though it was not incorporated into the food-additives amendment, the Senate report for that amendment said that safety ". . . does not and and cannot require proof beyond any reasonable doubt that no harm will result under any conceivable circumstance." That is really what we have been living with.

Zero risk is not possible. Zero risk, or the attempt to impose zero risk in food safety, does not recognize the limitations of science, and it does not capitalize on the strengths or the advances of science. It does not allow one to address, if you will, the real situation.

The definition of "safe" has come from the legislative history, administrative interpretation, and actual practical use. We believe that a definition of safe should be in the law; that it should, if you will, codify that which everybody, as you've heard for 2 days now, agrees is the way that safe must be applied in a regulatory mode. Therefore, the law should admit, in a codified way, that safe does not entail zero risk; that it is not an achievable nor even a desirable goal; and I think it would make clear to everyone, if it were so codified in the statute—in the agency as well as outside— that that is really not the goal, and that what we should be working toward, from both a scientific as well as a policy standpoint, is something else.

I think that there are a number of ways or sets of words to say that. I am not prepared—indeed, I am not sure that I am the one that can best finally determine what words convey that most accurately; that is, that safe has a very important meaning but it does not and cannot mean zero risk. A number of words have been used: insignificant, negligible risk, and the like.

What I think is important is that which we are trying to convey, to codify, and to announce to everyone in the form of legislation, if a definition is to go into the law. I think that words to do that should follow the concept.

The CHAIRMAN. Thank you.

Dr. Brandt, you are quoted in testimony submitted by another witness as saying:

> Risk assessment is not an appropriate approach to the problems of regulation. Rather, the real problem is that we simply do not yet have the appropriate scientific base to use risk assessment with full confidence in making many regulatory decisions.

From your quote, they go on to say:

> Using a negligible risk standard for regulating food additives, however, would require precisely what Assistant Secretary Brandt warns we know too little about to use reliably.

Could you respond to that?

Dr. BRANDT. Yes. In the first place, I do not think the quote is totally accurate. I happen to have a copy of my testimony right in front of me. It says, "Risk assessment is not an inappropriate approach to the problems of regulation." I believe that.

In the first place, I think that we have to recognize that there are still some valid scientific questions dealing with the appropriate use of quantitative risk-assessment techniques. At the same time we are trying to say, as the Commissioner is saying and other Commissioners have said, there are scientific issues that arise in our current process of regulatory decisionmaking.

This legislation would provide a structure, an opportunity, it seems to me, to begin to approach this problem of assessing risk in a meaningful, consistent, and sound fashion.

Now there are, as I said, valid scientific questions, but the Public Health Service currently has a number of research projects aimed at identifying and settling those questions. It will be an evolutionary process. I think that risk assessment at the present time is appropriate in a number of situations, and that it provides us with a stronger and more consistent approach than we have had.

The CHAIRMAN. In general, do you gentlemen—let's start with you, Dr. Brandt—agree with the principle for food safety reform as enunciated by the former Commissioners Kennedy and Goyan?

Dr. BRANDT. In general, as I understand from looking at their testimony, I would agree with them.

The CHAIRMAN. How about you, Mr. McMillan?

Mr. MCMILLAN. Yes, sir. I have not really studied the testimony. I have scanned it.

However, I would agree with Dr. Brandt.

The CHAIRMAN. OK. Dr. Hayes, it is important to have your viewpoint on that. Do you agree with that?

Dr. HAYES. Once again, having only read each of their testimonies once, I do agree with the principles in general. Indeed, as I have already mentioned, in some areas I think that it was said very well.

The CHAIRMAN. Dr. Houston?

Dr. HOUSTON. Yes, sir. I have had the opportunity of reading the testimony of both former Commissioners. I think the concepts that they embodied here are the same as was embodied by this working group.

The CHAIRMAN. All right.

Mr. McMillan, how would you respond to those who argue that the changes considered by the working group would weaken the law?

Mr. MCMILLAN. Nothing is static, Mr. Chairman. I think everything is subject to change. I would classify the food safety laws in that manner. They should keep pace with the new scientific information, with the new technology and the new techniques that are in place for us to use. Therefore, I would not categorize this as a weakening but, rather, a modernization, an updating of the food safety laws to keep pace with that scientific information.

The CHAIRMAN. Let me ask you this: What would be the consequences of not changing the food safety laws as they presently exist?

Mr. MCMILLAN. The consequences would be absolute frustration.

The CHAIRMAN. Is that what you were saying just now?

Mr. MCMILLAN. That is right. It is the fact that with the techniques, the technology, the scientific expertise that we have at this point and with the manner in which the food safety laws are structured, it is an extremely difficult thing to administer. Therefore, I guess frustration would be as good a word as any in terms of how you administer those food safety laws.

The CHAIRMAN. Dr. Hayes, how would you respond to that?

Dr. HAYES. I think that is absolutely true. It seems to me that the goal of food safety legislation and everything that prescinds from that is to provide and to assure a safe food supply.

When the law and its interpretation are such that one cannot recognize the limitations of or capitalize on the strengths of science, when one is in a position, as I mentioned in my testimony, of having to make a decision because of the law without even—because the law does not allow it—addressing the safety issue or the public health issue, it makes the agency, and indeed the Government, in administering the law oftimes look rather foolish.

When we as scientists are dealing with scientists outside the agency, using the same scientific principles and methodologies, and then suddenly we have to say, "Well, of course, that doesn't matter. We cannot use it because the law doesn't allow it. We will have to decide on another basis," that is frustrating, to say the least.

The CHAIRMAN. Dr. Houston?

Dr. HOUSTON. I certainly agree that if we do not make some changes, we are eventually going to build a house of cards that will fall down upon us as we reach decisions that are simply not consistent with the scientific information that we now have and which is going to build in front of us in the years ahead.

The CHAIRMAN. How about you, Dr. Brandt? Do you feel the same way as the other three gentlemen here today feel?

Dr. BRANDT. Yes, I do.

The CHAIRMAN. Now the point I am making is that it seems to me if you continue to apply a zero risk standard, in light of present scientific technology, which is widely expanded since the original Delaney clause came into existence, you will run into difficulties that are insurmountable as far as even insuring a food supply to some people in some areas.

Am I wrong? Is that too strong a statement?

Mr. McMILLAN. No, I think in general you would be correct, Mr. Chairman.

The Chairman. Does everybody else agree with that?

Dr. HAYES. Yes.

Dr. BRANDT. Yes.

Dr. HOUSTON. Yes.

The CHAIRMAN. Do FDA and USDA need any additional legal authority to assure a safe food supply?

Mr. McMILLAN. It is not a question of additional legal authority. Really, I think there is ample legal authority present. It is a matter of clarifying and codifying the present laws in terms of modernizing them and bringing them up to date in terms of the modern-day science and technology we have been discussing.

The CHAIRMAN. Does the decision in the *Monsanto* case obviate the need for changing our food safety laws? Dr. Hayes?

Dr. HAYES. No, I do not believe that it does. At least it certainly does not mean we should not discuss the possibility of legislative change in the various areas that we have discussed.

The *Monsanto* decision, in fact, and an interpretation of that 1979 decision, is not that FDA has discretion under the Delaney clause to ignore a de minimis risk. What that decision, in fact, said was that FDA had the discretion under the food additive definition to ignore a de minimis migration into food of a food packaging component. In other words, what the court was saying was that if it is a very small amount with negligible or de minimis risk that is migrating from a packaging material to food, we at FDA did not have to consider it a food additive. Therefore, we did not have to apply the Delaney clause or whatever rules that apply to food additives. It was definitional.

The CHAIRMAN. Therefore, in all other food additive situations you would have to apply Delaney?

Dr. HAYES. That is exactly correct. Whether the principles from the *Monsanto* case could be applied more generally is something that has not been tried nor tested.

The CHAIRMAN. Tell me, Dr. Hayes, how and when does FDA use risk assessments in food safety decisionmaking?

Dr. HAYES. We use risk assessment in a number of decisions, although, as I am sure you are aware, risk assessment is not the only means or the only tool that is used in making decisions about food additives, whether direct or indirect, intentional or not.

There is no question that many aspects of risk assessment are aborning. We are learning—that is, the scientific community is learning more and more—how to use risk assessment. It is not accurate to say that we do or, indeed, can use it across the board, or even that it would be appropriate to do. That it would be possible scientifically to do it evermore, I believe is true.

The CHAIRMAN. When should risk assessment be used in food safety decisionmaking?

Dr. HAYES. I do not think I am prepared at this time, Mr. Chairman, to tell you in exactly which cases or which sorts of cases. I think that there is no question that risk assessment, if indeed we had absolute liberty to use it, could be used evermore in decisions about food additives. It certainly is already used in a number of areas, such as in pesticide residues. It is used in areas of the so-called nonintentional additives or components—aflatoxins, for example, that are there and not intentionally added. Risk assessment can be used there.

I think it could be used even more widely, but it is not necessary to use it at all times. It is true that we have not yet the capability, though it grows every day, to use it in every situation.

The CHAIRMAN. Yesterday the chairman of the NAS Panel on Risk Assessment urged the development of guidelines for the use of risk assessment methodologies. Does the FDA have such guidelines?

Dr. HAYES. We do not at this time, although we are well aware of the NAS report. Indeed, we were involved in organizing it. It is something that we at FDA have been and continue to work on; that is, guidelines and ways to approach risk assessment; the appropriate way to implement them; the appropriate way to keep them current, if you will; and, most especially, the input of outside groups. There were some suggestions from the NAS, as you know, about the kinds of guidelines and the way they could be tested or affirmed before they are put into practice.

The CHAIRMAN. Let me ask the panel this, and it is probably more appropriate for Mr. McMillan and Dr. Houston, but I would like any or all of you to comment:

If we continue down the road of zero risk within the present interpretation of the Delaney clause, what type of foods that we all consider acceptable today would you have to outlaw?

Mr. MCMILLAN. What I would like to do is start with Dr. Houston and then proceed on down the table with responses.

The CHAIRMAN. Give us some illustrations of food that everybody accepts today that would have to be outlawed, even though there is really little or no risk, probably no risk, to human beings.

Dr. HOUSTON. Well, for example, black pepper might go by the wayside. If we were to take the zero risk concept, we could run into problems, of course, with aflatoxin in peanuts, if we were not able to use tolerances and risk assessments.

The CHAIRMAN. That means we would have to ban peanuts?

Dr. HOUSTON. Absolutely. We also find aflatoxin in other grain crops, such as corn, for example, where tolerances now exist. If we were to apply a zero risk concept, we might find those food supplies taken away from us.

Those are some examples of what might occur if we take the concept of zero risk and apply it across the board.

The CHAIRMAN. Do you consider there to be any danger in eating black pepper or corn or peanuts?

Dr. HOUSTON. Well, I usually eat those foods every day in one form or another. I have no problems about the safety of those foods. I guess, like everyone else, I have to eat every day, too.

The CHAIRMAN. Would you consider it bizarre if you had to ban those foods?

Dr. HOUSTON. Certainly. Absolutely.

The CHAIRMAN. Give us some other illustrations. I just think it is important for people to realize how ridiculous the zero risk interpretation can really be under rigid circumstances.

Dr. HAYES. There are risks, as you know, Mr. Chairman, in the inclusion of certain compounds. As we have more evidence or as we have the ability to detect them, it can, indeed, seem bizarre, at least to the average American regarding his or her eating habits.

I only learned recently that tarragon vinegar would have to be put on that list, which I think would be of concern.

Not only are we talking about specific foods, but I think very important, though not as readily apparent, are various food additives that may have a very important functional use; that is, to prevent the growth of bacteria, for example, very harmful bacteria, in certain foods, or those that are used to make foods palatable.

The CHAIRMAN. What you seem to be saying is that if you apply a zero risk standard, you may have to take various additives that are very beneficial for mankind off the market under a rigid theory which in some respects, you have had to apply.

Dr. HAYES. Not only that, but one that has been accepted because we did not know or could not confirm it was there. If, indeed, the analytic techniques allow you now to find it in a very much smaller amount, one trillionth rather than one billionth, and the like, then you may have to change your decision. Something that was OK because you could not find it—now, if you can find it, by definition it is present, and therefore you may have to do something. There is no question that there are many compounds that have, however infinitesimal, the ability to cause cancer in some animal species or at some dose or some exposure.

Indeed, if you can find these as analytic methodologies move along, then obviously you have to do something if you are constrained by a zero risk, yes-no situation, rather than looking at the public health implications, what is the risk, how much is really there.

The CHAIRMAN. So some of these compounds you basically consider to be without risk, but because of the scientific methodologies and techniques and systems that have been developed, you can reach a point where you can rule out many, many things that are totally safe because carcinogens may show up in parts per trillion.

Dr. HAYES. Well, it is even worse. With the example that I gave you of the flavor, cinnamyl anthranilate, indeed, there was no reason for us to look at the risk or the public health implications of that compound, that additive. Because we could find it and it otherwise fell under the definition, we would have to ban it under the

Delaney clause. Looking at the public health implications, since it was irrelevant, would have only consumed resources unnecessarily.

The CHAIRMAN. Dr. Brandt, can you give us some examples of foods that would be banned that you consider to be healthful and helpful to the American citizens?

Dr. BRANDT. I personally like greens with vinegar on them, and that bothers me, I think.

The CHAIRMAN. I think of the old home remedy for arthritis; a lot of people would be really up a creek if they could not get their vinegar.

Dr. BRANDT. I think it is important, Mr. Chairman, to recognize that science is continuing to move. Our ability to detect more and more substances in trace amounts, in very small amounts, and particularly to define weak, weaker, and even weaker carcinogens—that is, substances that may very well lead to genetic change or other kinds of changes that would potentially lead to a malignancy in some species—is going to get more and more sophisticated.

The CHAIRMAN. It is plenty sophisticated now, as I understand.

Dr. BRANDT. It is plenty sophisticated now, but it is going to get even more so. As it does, that means more and more foods that are important also will be added to that list, if a zero risk standard is applied.

I think it is not just the fact that we have a lot of foods today, like black pepper and peanuts, and so forth, that would have to be banned, but more and more will be added as we move down the road.

The CHAIRMAN. Mr. McMillan?

Mr. MCMILLAN. May I add one underscore to a comment that Dr. Hayes made? That is the question of whether or not something is truly cancer causing in man. It may be in whatever quantity it could cause cancer in animals, but under scientific determination that does not necessarily mean that it causes cancer in man. That is an important element that goes through this whole question of the no risk and the zero concept.

The CHAIRMAN. I will make this my last question because I want my colleagues to have an opportunity to ask you questions as well. This is an extremely interesting issue for me. I believe that all of you are dedicated to having strong food safety approaches in our society, as I believe former Commissioners Kennedy and Goyan and other scientists who have appeared before us have been.

However, some scientists have expressed to me that if you have to ban on a zero-risk basis any foods which have food additives or effective compounds which have any amount of carcinogenic material in them, no matter how infinitesimal it may be, that that would affect almost everything. Is that a wrong interpretation or is that just too bizarre?

Mr. MCMILLAN. That is pretty far out, Mr. Chairman, but of course it is not out of the realm of possibility.

The CHAIRMAN. Particularly as one gets into greater science.

Dr. Hayes.

Dr. HAYES. Only as I suggested earlier, as the analytical capabilities and the testing methodologies advance, we are finding more and more chemicals that are in the food supply, whether put there intentionally, whatever important uses they have, or they are there willy-nilly. It seems to me that it is irrational as well as anti-intellectual—and forgive the strong terms—to say that none of that matters, and that if at any dose under any circumstances a particular chemical causes cancer in an animal species, and if you can find it with evermore precise analytic methodologies, then you have to do something about it, then I am not quite sure why we talk about public health and food safety, because that is the one ingredient that often is left out—indeed, as I have mentioned and cited examples, it is the one that is left out, because it is irrelevant. I think when you get to that point something is wrong.

The CHAIRMAN. Thank you.

Senator Quayle.

Senator QUAYLE. Thank you very much, Mr. Chairman.

I welcome our panel.

Thank you for these hearings. This is the last day of these hearings. I think that so far they have been very productive. We have three distinct, diversified groups testifying today to sort of put a cap on what we have had all week.

The question that is going to be before us is, Should we do anything legislatively and, if so, what? I gather from the testimony and the remarks that you have made to Chairman Hatch that, if I could refer to page 3 of Mr. McMillan's testimony, under the title of "Latest Thinking," where you identify the term "safe," the Delaney clause, the risk-benefit assessments, the scientific review processes, and phaseouts—that those are the general areas in which you agree something ought to be done legislatively; is that correct?

Mr. MCMILLAN. These I would classify, Senator, as the major things that should be addressed first. There could be some lesser things that should be considered, but these would be the major items.

Senator QUAYLE. If these would be the major items, are these major items that need to have legislative attention and legislative change?

Mr. MCMILLAN. In our considered judgment, yes.

Senator QUAYLE. Do you agree with that, Dr. Brandt?

Dr. BRANDT. Yes.

Senator QUAYLE. What about the argument or the idea that these major areas that I just announced, and you put in your paper—why can't they be done regulatorily and within the administration? I believe before the Congress is going to act that we have to be convinced beyond any reasonable doubt that current law is simply inadequate, that you cannot do it regulatorily, that you must have new legislation. We have to be convinced of that. I have yet to have really definite testimony from anyone—although the former Commissioners Wednesday both came out and said legislative—but I had to draw it out of them, like I am having to draw it out of this panel right now—coming before us saying, "Look, fellows, the law is inadequate. We can't do it administratively. Therefore, you've got to change it. Here's what needs to be done."

Now why can't you do it regulatorily in the executive branch?

Mr. MCMILLAN. There is a school of thought that the regulatory approach, under present statutes could take care of the problem. However, I think, as we have been discussing in the question-and-answer phase, particularly with Chairman Hatch, we are going to be constantly frustrated along the road because the law is based upon the 1950's and 1960's technology and scientific information. That was passed in good faith obviously. But today we are talking about an entirely different situation with new techniques, with the ability of finding things that were not thought to be there when the last laws were passed or the amendments to the Food, Drug, and Cosmetic Act were passed.

Therefore, although we can talk about administrative changes which are always subject to change, too, as people come and go within Government, if we have a statutory basis, it gives much better opportunity for continuity in administering the laws.

Senator QUAYLE. Are you saying you cannot do it administratively? Is that what you are saying?

Mr. MCMILLAN. Essentially, yes.

Senator QUAYLE. You are saying yes, Mr. McMillan.

Dr. Hayes, do you agree you cannot address these problems that have been outlined with the regulatory process in the executive branch of Government?

Dr. HAYES. I think for some of them there is no question you cannot do it from an administrative mode. Indeed, the very first issue—that of codifying what safe does and does not mean with respect to risk and the like—has already been done administratively, since it is nowhere defined in the law since 1958, and it has led to problems. That is why we think it should be codified in the law.

With respect to the Delaney clause, as I mentioned, we have already had specific problems, and we do not know, at least at this time, of an administrative out.

I remind you of the saccharin case, where at least at that time my predecessor did not feel there was an administrative way to do that which people thought ought to be done, and the Congress literally exempted it from the Food, Drug, and Cosmetic Act by putting a moratorium on any ban. Clearly, there it took specific legislation to enforce the will of Congress because of a law that was there, and nobody at that time, apparently, or since, has found any other way to handle that problem under the current statutes.

I think that there are some other areas where there may be administrative ways to try. Indeed, in a number of areas we already have done that with what is known as the constituent's policy. We have already discussed de minimis with respect to the definition of a food additive and whether it should be treated that way under the de minimis rule for an indirect additive, that which is leached or migrates from packaging materials.

However, I think that the problem is that some of these things have not worked. Some of them, indeed, from an administrative standpoint I think would be difficult to do, and I think would consume a terrific amount of resources trying to do it that way. To say that we have not tried or will not continue to try is not true, or to say that we have not had successes in the past, but there have been notable failures as well.

Senator QUAYLE. Do you believe that the present interpretation of "safe" as you have interpreted it is inadequate?

Dr. HAYES. No. I think the way that we have interpreted it in the FDA is appropriate. We have not interpreted the term "safe"—

I am excluding Delaney—as a zero-risk standard. However, it has given rise to problems. It has certainly given rise to misunderstandings or misapprehensions on the part of people outside of the agency as to how we will treat it, what does the law really mean.

I think that to codify what "safe" does and, by definition, does not mean in the law itself would be a very great help. That obviously cannot be done administratively. We have gone as far as we can administratively. Someone else could have a different interpretation in terms of administration. A successor of mine might feel differently, or there might be other changes that would lead to a different administrative interpretation. There is no control over that outside of legislation.

Senator **QUAYLE**. Do you agree with these five general principles Mr. McMillan outlined, that those are the ones that need to be addressed legislatively and cannot be addressed adequately through the regulatory agencies?

Dr. **HAYES**. For all of them, I will not say cannot unequivocally because some have not been tried. I think in general that is true.

Senator **QUAYLE**. For which one of those five do you think that we absolutely need legislation, that you cannot do it regulatorily?

Dr. **HAYES**. We have already gone as far as we can in terms of adding a definition of "safe." We have done everything that is possible.

Senator **QUAYLE**. In other words, the definition of "safe," that definitely—Congress has got to deal with that?

Dr. **HAYES**. That's what we feel——

Senator **QUAYLE**. What other one?

Dr. **HAYES**. We think that it would be desirable to change the Delaney clause consonant with the science that we have already talked about. I think the same is true for utilization of risk-benefit.

Concerning use of outside scientific review and advisory committees, I think it would be helpful for that to be codified in the law. To say that you cannot get any scientific advice without the law obviously is nonsense. I think it would be helpful. It would tell people exactly how outside science will be brought to bear or would be used by the agency, rather than their not knowing just what we might do at any given time.

As I understand it—I am not a lawyer, but as I understand it—there is no authority for gradual phaseout now. Indeed, in the past the Department of Justice has said that we are not allowed to use that.

Senator **QUAYLE**. Then you are saying that the first three—"safe," the Delaney clause, and the risk-benefit—are rather imperative; that you cannot deal with them adequately on a regulatory basis?

Dr. **HAYES**. I think that is true of No. 5, the phaseout as well.

Senator **QUAYLE**. You think that is also true of No. 5; that you cannot deal with those issues from an administrative or regulatory basis?

Dr. **HAYES**. Yes, sir.

Senator **QUAYLE**. Would you like to have help on determining the independent scientific review processes?

Dr. **HAYES**. That is correct. I think these five, as Mr. McMillan said, are the linchpins. They are the cornerstones. There are other areas that the working group and others outside the Government have looked at very carefully over the past few years that I think are important and that would have to be changed legislatively from a legal standpoint. I do not think they are as important as these which are clearly core to food safety.

Senator **Quayle**. However, what we need to pin down is an exact statement from you, and I think that we have gotten it, that you cannot do these particular areas any more by regulation, and that it has to be done by legislation. Is that accurate?

Mr. **McMillan**. I would say yes, sir.

Senator **Quayle**. Would you agree with that?

Dr. **Hayes**. In general, it is, though I only add the caveat that——

Senator **Quayle**. We do not want to get too many "buts" in there.

Dr. **Hayes**. No, only that some of these we have not tried. To say that something is not possible when it has not been tried, I do not know, but I think that the principle which you enunciate I subscribe to.

Senator **Quayle**. OK. Now, then, if that is the case, Dr. Brandt, when will we be seeing this legislation on these particular points from the administration specifying some of the concerns that are outlined here? Is there any timetable that you can enlighten us with?

Dr. **Brandt**. We do not have a time table that I can give you at the moment, Senator Quayle. We are, in fact, still studying the issues in terms of the specifics. As Dr. Hayes testified, the words become important, and we want to be sure they are correct.

Also, as Mr. McMillan's testimony indicates, at the present time these positions that are included in his testimony, in fact, have not received official action. They have never been accepted nor rejected as official administration policy. Until those things happen, clearly we will not be sending up any legislation.

Senator **Quayle**. I wonder if——

Mr. **McMillan**. May I——

Senator **Quayle**. Wait a second, and then you can respond.

I wonder, Dr. Brandt, if legislative relief is what basically Dr. Hayes and Mr. McMillan were talking about—they said it is essential; they said that it is needed—I wonder when you think you might either reject or accept from an administration point of view some of these legislations. Is it going to be this year, next year, 1990, what? What are we talking about? You have to give us some idea. If you cannot give us a specific idea, guess. [Laughter.]

Dr. **Brandt**. Well, I cannot give you a specific idea, and my guesses do not always turn out to be right.

Senator **Quayle**. Go ahead and pontificate. This is an open hearing. No one will hold you accountable. [Laughter.]

Go ahead, Dr. Brandt.

Dr. **Brandt**. My guess is that it would be soon, sir. [Laughter.]

Senator **Quayle**. Now is that a scientific determination of "soon"? Would that lead us to believe this year, "soon" according to the latest scientific data that we may have on this issue, definition of "soon"?

Dr. **Brandt**. It is as precise as——

Senator **Quayle**. I mean is this a priority?

Dr. **Brandt**. It is as precise as we can be right now.

Senator **Quayle**. Is this a priority within the administration or are you just sort of testifying here today because we asked you, and there is not going to be a whole lot of push and momentum? I would like to get a feeling.

Don't take the microphone away from him—speaking to Mr. McMillan. [Laughter.]

We will let you speak.

Dr. **Brandt**. The USDA is trying to exert their primacy in this issue, I think, that is why he is taking the microphone.

The issue is important to all of us, because we are concerned about food safety, and we are concerned about trying to get this done. This working group has been working on this issue now for approximately a year and a half or a little longer. It is a very complex issue. We clearly do not want to come up and propose to you changes to make the food safety legislation consistent with modern science and consistent with modern thinking without being absolutely certain that it is. That is going to take some additional time.

Senator **Quayle**. OK, Mr. McMillan.

Mr. **McMillan**. Senator, as we looked at the food safety laws, we addressed legislation that had been introduced previously by Senator Hatch and others in the House. As I have stated in the testimony, we look forward to working with the committee and the committee staff, with industry, consumer groups, and the scientific community, in trying to put together the best consensus in terms of changes in the food safety laws.

We have no intention to present to the Congress a specific bill that the administration advocates.

Senator **Quayle**. The former Commissioners—I guess it was Wednesday—in this line of questioning I pursued with them as well—they said that the actual legislative language should be rather at a minimum. In other words, the policy orientation, but what would really be helpful to them would be the legislative intent, the record that is documented that goes into any kind of legislation. Therefore, they recommended to us—in some of the same areas that you are talking about—they said that it should be rather general. I have pointed out that it is going to be very difficult to get in a debate on the floor of the Senate, let alone in the committee, on some of the scientific data that we have had. We would be out in left or right field, whichever place you want to come from on that.

However, do you agree that that is the kind of legislation that we ought to be pursuing and that the real importance and the meat of it would be within the legislative record and the legislative intent that would accompany any legislation?

Mr. **McMillan**. It is always difficult to respond to a question of that sort because legislative history is always a part of what happens after a statute becomes law. The courts and others will take the report, for example, and the floor debate as a basis of legislative history.

However, I have always been one who felt that if you can become more precise within the statutory language itself, is much easier from an administrative viewpoint to administer a law rather than have to rely upon the legislative history.

Of course, as Dr. Hayes has said, the "safe" application comes from the legislative history rather than the statute itself. That caused a lot of grey area that the administrators of the laws has had to work with.

Senator **Quayle**. I have two more questions, Mr. Chairman, and then I will yield.

On defining this acceptable risk, it has been suggested that perhaps one in a million is an acceptable risk. Would that be an acceptable risk for you, Dr. Hayes?

Dr. **Hayes**. I do not think I can say that it is an acceptable risk across the board, but I think there is no question that in a number of areas for a number of substances that, if properly understood and interpreted—and I understand there was a discussion of what that does and does not mean with the committee yesterday—then I think that it can make very good sense. However, to say that that is the absolute number, if you will, to be applied, never less, never greater, I am really not prepared to say that, but I think it makes sense.

I am not an epidemiologist nor a statistician, to explain what the interpretations are and, more importantly perhaps, as you heard yesterday, what they should not be, but I think that it has been accepted by many that in frequent situations that makes sense.

Senator **Quayle**. Let me just add this point to that question that is going to present a political problem, whether it is more, less, or any precise definition of what "acceptable risk" is. Let's take, for example, that you have one out of a million. That means that there would be 200 cases of cancer which you are going to permit. Therefore, you are going to increase the risk of cancer. From a political point of view, public interest, public concern, that is not a very pleasant thought, nor a pleasant position to be in.

I just wonder, as we make this exact determination, getting beyond the parameters of the executive branch and looking at it in the public arena, the public interest, and the public concern, how you might suggest that we deal with this.

Dr. **Brandt**. Senator, in the first place, having risk of one in a million, as has been proposed by several of the people testifying here, does not mean that one out of every million people will get cancer. In fact, that is only a probability; it is not an actuarial statement that they are talking about. It is a general statement having a probability of that level, but it will not result in the actual existence of 200 or so cases. Indeed, that would be the absolute worst case, if that were to happen. I think those two things have to be kept somewhat separate.

Nobody is advocating—or I do not think any of the people testifying were advocating—that we will accept 200 or 5 or 3,000 cases of cancer, but rather to say that one has to accept the probability level at some point that is reasonable.

Senator **Quayle**. Let me just follow up, demonstrate, and emphasize the problem. I know exactly where you are coming from. You say it is probability rather than actual or actuarial.

However, the point is, by any determination on a number basis, there is going to be—you can make that allegation. Since you are coming off of this saying that we are for zero risk, we are not for cancer, at some point you are going to allow, by this definition, certain cases of cancer at an acceptable level. If it gets into that dialog, and I think it could very well get there, then it makes it exceedingly difficult from a public official's point of view to deal with that.

That is why I am asking you, and bringing this question up, for a little bit of guidance on how we are going to be able to respond to that issue, or is there another mechanism that we can use to deal with this that would get to the same place without—and I get back to the question I asked Mr. McMillan—this exactness. When you come out with this exactness, whatever it is going to be, you are going to get that kind of allegation.

Mr. **McMillan**. I do not doubt in the least that in this somewhat irrational and emotional world we live in that those charges would. The position we are advocating at this point, and those advocated by the previous Commissioners and by most of the scientists who have testified before you, is that we are not by these changes going to increase exposure to those substances. We prefer to get out of the position we are now in of having foods and other substances out there that do not meet the current legal requirements. We can approach it in a much more sensible, much more scientifically sound basis.

Nobody is advocating suddenly throwing carcinogens into the food supply. Nobody would go along with that. Simply because you detect something at .06 parts per trillion and it is a weak carcinogen that occurs in only one species of mice it is not necessarily automatic that it is going to do the same thing in humans.

Senator **Quayle**. I have one final question, and then I will yield.

Mr. McMillan, there has been some discussion, information that we have at my office, on the job being done on the problem with pesticide residues on fruits and vegetables, residues in meat. There is a question on the enforcement. There is a question on the accountability. I wonder if you might address this. Is this a big problem? Are you dealing with it? I am sure you are aware of it. What would you say to some that may raise the question that there is simply inadequacy in this particular issue?

Mr. **McMillan**. You are right, Senator, there has been a great deal of discussion about, what is claimed as inadequacies in the residue testing program that exists in the case of meat and poultry inspection. Those claims are, I think, grossly in error, because we are in fact, carrying on a sustaining residue testing program through our meat and poultry inspection program. Dr. Houston is the Administrator of FSIS. I would like to have him comment a little bit more precisely on it.

Senator **Quayle**. Can you tell us what you are doing as far as——

Dr. **Houston**. In fact, we testified yesterday in the House about that particular program as it relates to imported meat before a subcommittee of the House Agriculture Committee. They explored the matter indepth.

We do carry out random sampling of meat and poultry, both domestically and that which is imported, for a whole variety of chlorinated hydrocarbons, organophosphates, antiobiotics, environmental contaminants, trace elements, and hormonal substances.

We will take up to about 50,000 samples a year, both on a random basis as well as through a directed sampling program. We are essentially carrying out the same degree of regulatory intensity today that we were 4 years ago, and there has been no cutback, no diminution, in that program whatsoever.

Senator QUAYLE. Thank you, Mr. Chairman.

The Chairman. Senator Grassley?

Senator GRASSLEY. Mr. Chairman, I am going to have to apologize because I am not going to be able to stay throughout the entirety of these hearings, as I did on Wednesday and Thursday, but I do appreciate the opportunity to be here for a short time this morning. I do have questions and comments at this point that I would like to pose to this panel.

I would like to suggest that probably the establishment of the safety group that you are on had a multitude of assignments, of things to work for, and reasons for working for changes in the safety laws.

However, I would like to ask if, from the standpoint of this administration. Learning from the past, if in and of itself the nitrite fiasco—constitutes reason enough, for changing food safety laws and for changing some administration within the various agencies that deal with food safety, irrespective of changes in law?

Mr. McMILLAN. Senator Grassley, I would cite the nitrite issue as only one of a number that we have talked about, such as saccharin, and so on.

Senator GRASSLEY. But I am asking you now if that isn't reason enough, besides all the other reasons you might have.

Mr. McMILLAN. That certainly brought a great deal of focus on the problems that we have been addressing today in terms of administering the food safety laws.

Since the nitrite issue did address the question of primarily cured products, largely pork products but beef as well, I think Dr. Houston, as Administrator of Food Safety and Inspection Service, would be able to shed some additional light on that.

Dr. HOUSTON. First of all, let me just cover some of the points which are part of our latest thinking. It was on page 3 of Mr. McMillan's testimony.

For example, at the time that the incident occurred, you may recall that the Attorney General issued an opinion that the Department of Agriculture did not have phaseout authority should nitrite in fact be found to be carcinogenic and regulatory action taken. That is part of one of the issues we have here today, whether to authorize gradual phaseouts rather than immediate prohibition of substances that do not meet the safety standards. That is a needed statutory requirement that we do not have today.

Also at that time, there was no statutory basis to use independent scientific review processes in making food safety decisions. We are saying today that it ought to be put in the statute, and that authority should be there for HHS and USDA to utilize.

There was no opportunity to utilize risk-benefit assessments in determining whether to prohibit the use of food ingredients, at least as related to nitrite under the USDA statute.

I am citing at least three provisions today that would have been useful to the Department of Agriculture and to the Food and Drug Administration had they been in place when the nitrite situation was in front of the Government.

Senator GRASSLEY. Dr. Hayes, have there been any administrative procedures that have been changed within your agency as a result of that, so that there would be further review and proper perspective given to studies that might suggest things that really do not have a scientific basis as originally anticipated?

Dr. HAYES. Indeed, and while I was not Commissioner when this question arose, there is no question that we have established and, in some cases, modified already established procedures in terms of the verification of scientific information, how that is used. That is, on the one hand, that one not presume something that is not verified; on the other hand, that one not wait too long under the presumption that it is not important.

Indeed, it is at least part of the reason that one of the suggestions that this group has made today is that—and for everybody to know in the statutory language the provision—when the FDA or the Secretary of the Department feels it appropriate, to get outside opinion; that is, to get expert scientific opinion on the quality of studies or what, in fact, they mean in terms of interpretation, should they be repeated, and the like.

I think the bottom line is, yes, we have learned from that experience.

Senator GRASSLEY. You are saying that there is a need for change in the law for you to accomplish that, or you would just like to have it statutorily set out so that it would be certain to be followed?

Dr. HAYES. Current law allows us to elicit and to utilize outside expert opinions, scientific and otherwise. Therefore, we do not need a law for that, as I mentioned to Senator Quayle a few moments ago.

I think that if one rather carefully defined in a statute that such information was available, under what general conditions of discretion it would be utilized, what kinds of questions, significant ones perhaps relating to carcinogenicity and the like, then I think everybody would know how such information was going to be treated.

Senator GRASSLEY. I anticipate testimony from successor witnesses that will establish that the nitrite controversy is a serious case in point for the need of the change in the food safety laws and giving them flexibility—and others dismissing that on the basis that since nitrites are not now a carcinogen, that we ought to look at that particular episode as merely hypothetical and probably not strong enough to warrant food safety law modifications.

I am glad to hear that you feel that that is very definitely an episode that we can learn from. I think from my standpoint and that of my constituents—and I am not talking just about pork producers, either—they consider the incident a costly nightmare and not merely something hypothetical.

When you consider causing harm to the agricultural sector, the possibility of throwing thousands of people out of work, or the possibility of harming our Nation's family farmers, it is irresponsible not to learn from that because of the harm that it does or that it did to the consumer. The consumer is not served because of the fear of botulism and just generally giving them a false impression that the banning of something is eliminating that danger altogether.

You see, I do not think we can look at these things as being merely hypothetical. Later on this afternoon we will have some testimony from the National Pork Producers Council. I likely will not be able to be here for it, but I believe we will learn of the economic impact that the nitrite scare did have upon the agricultural industry.

I am thankful that the economic harm is a short-term harm and, hopefully, we have prejudiced only one generation of consumers of meat with fears which are unjustified. Again, this goes beyond something merely hypothetical. It really has turned into a situation by which we must learn.

I appreciate very much the direction that your group has taken, all of you who testified here. I also appreciate very much that this nitrite fiasco is a case in point by which we learn and do not repeat the mistakes of the past.

I think all the questions I would have asked, unless there is some response to what I just said from anybody on the panel—my questions were pretty much covered by Senator Quayle.

The CHAIRMAN. Thank you, Senator Grassley.

I want to thank you, gentlemen, for appearing before us today. Your testimony has been most helpful to the committee. We appreciate the efforts that you put forth in preparing your testimony and, of course, delivering it here today.

Thank you for coming.

Mr. McMILLAN. Thank you.

[Additional questions submitted by Senator Hatch to Mr. McMillan follows:]

ADDITIONAL QUESTIONS FOR DR. MR. McMILLAN PREPARED BY SENATOR HATCH

1) Saccharin was mentioned frequently during the hearings. Please describe for the record research on saccharin conducted since 1977 when FDA proposed the ban.

2) During the hearings, reference was made to the risk of one in one million per lifetime (1×10^{-6}). Please explain what this means?

3) It is frequently said that quantitative risk assessment almost certainly overstates the actual risk because of the conservative assumptions used. Please describe these assumptions and why they are conservative.

4) Please identify the ways in which FDA and USDA have used risk assessment during the last 5 years. Describe each regulatory decision which was based on a risk assessment or other instances in which risk assessment was conducted.

5) Please identify the instances involving the regulation of food (including additives and contaminants) in which scientific issues were referred to a Committee, task force, working group, etc. for advice. Describe the timing of the referral, the advice given and the outcome of the matter.

6) In 1958, the Department of HEW testified on the food additive amendment to the effect the Delaney Clause was "redundant" with the general safety standard for food additives because scientists could not establish a safe level of use for any substitute shown to induce cancer in animals. Is the Delaney Clause still considered to be "redundant" or does it now mandate decisions that would not otherwise be made. Please give examples if possible.

Note: No reply to questions had been receive by press time.

The CHAIRMAN. We will now hear from representatives of five consumer interest groups. We will begin with Mrs. Carol Tucker Foreman, who will testify on behalf of the Consumer Federation of America. Following Mrs. Foreman, Public Voice for Food and Health will be represented by their executive director, Ms. Ellen Haas. We will then hear from Mr. William Schultz, attorney for Public Citizen Health Research Group; followed by Dr. Michael F. Jacobson, the executive director of the Center for Science in the Public Interest. To conclude the consumer panel, we will hear from Mr. Arnold Mayer, who is the international vice president for the United Food and Commercial Workers International Union.

We are delighted to have all of you here today. We look forward to taking your testimony at this time.

We will begin with you, Mrs. Foreman.

If I could mention this before you begin, I want to thank you in advance for the thought and the efforts you have put into your oral and your written testimony. I might mention that all of your written statements will be placed in the record as though fully delivered here. We have asked in our letters to you and our chats with you that all witnesses for the remainder of the day, including consumer witnesses and industry witnesses, limit their comments to no more than 5 or 6 minutes, to allow time for questions. I think the questions are probably more important than anything else.

Mrs. Foreman?

STATEMENT OF CAROL TUCKER FOREMAN, PRESIDENT, FOREMAN ASSOCIATES, REPRESENTING THE CONSUMER FEDERATION OF AMERICA

Mrs. FOREMAN. Thank you, sir.

I am Carol Tucker Foreman. I serve as an adviser on food and nutrition issues to the Consumer Federation of America. I am here today to represent that group.

From 1977 to 1981, I was Assistant Secretary of Agriculture for Food and Consumer Services with responsibility for enforcement of the Federal meat inspection law and Poultry Products Inspection Act. During that time the Government had to deal with the issue that nitrite might be a carcinogen. The most common use of nitrite is in processed meat products. In that use it is not a food additive under the Food, Drug, and Cosmetic Act, but is a so-called prior sanction substance and is, therefore, regulated under the Federal Meat Inspection Act. As a result, I have spent a fair amount of time dealing with some of the issues that you raise here today.

Over the past 2 days, and again this morning, you have heard a great deal about the troubling aspects of the food safety laws, why they have bedeviled FDA administrators, Members of Congress, and the food industry. It has not been much noted that the laws have been very successful in carrying out their intended purpose. They have protected the American consumer. That is the first and primary purpose of the laws, and I think it is fair to argue that they should not be unduly burdensome on industry in the course of protecting consumers. I do not believe that it can be shown that they have been unduly burdensome.

We have a very abundant, very safe supply of food in this country, usually available at reasonable prices.

Before the Congress rushes headlong into sweeping changes, I think you should have some very specific information on how much trouble the law with regard to food additives has been. Has the present zero-risk standard really been so hard to live with?

Since passage of the Delaney clause in 1958, only a very few substances have been taken off the market. None of them seem to have been absolutely essential to the food supply. It would be useful for Congress to ask the industry and the Government to provide a detailed explanation of what has been lost by their absence, what foods are not now available that might have been, what nutritional value has been forsaken, what safety value has been denied. I think it is fair to ask for a list, in addition, of those food additives that might be removed from this food supply in the future and an explanation of what that might cost. If you will ask me, I will come back to elaborate later on the difference between basic commodities and food additives, which the Commissioner of the Food and Drug Administration doesn't seem to understand.

Finally, we should know what substances are now being marketed that are in jeopardy in the future. What is their loss going to mean to us? If there is a large number of substances that are carcinogens, perhaps the law ought to be changed. If there are only one, two, or four, perhaps we should handle them with exceptions to the law, as you have done in the past.

That course is hard on lawmakers and it is hard on law administrators, but it has worked very well for the public, and the public should come first. CFA opposes any change in the law that will lessen consumer protection.

However, if Congress feels compelled to change the law and abandon the zero-risk standard, I think it is imperative that you be very, very specific about what that new standard will be. Bills introduced since 1981 have left standard-setting to others. That is convenient for you, but it is also fraught with peril.

Assessment of risk is a scientific process. Setting an acceptable level of risk is a political process. It requires making a judgment between the interests of competing groups within society. It is a job that should be done by the elected representatives of the people.

When Congress is uncertain, it frequently passes statutes that have vague language telling an agency to please just get the job done. Letting experts decide what the people's representatives find too hard to decide, I think is an endorsement of paternalism over democracy.

Congress has been very specific in some laws that you have enacted. You have found it possible to set a specific level of particulates of carbon dioxide that can come from automobile emissions under the Clean Air Act. You have set lead standards in gasoline. You have set a 55-mile-an-hour speed limit because it saves several thousand lives a year. I think that you should also be prepared to say how many cases of cancer are negligible or insignificant.

Justice Douglas once said, "Unless we make requirements for administrative actions strict and demanding, expertise, which is the strength of modern government, can become a monster which rules with no practical limits on its discretion." I think we would all be wise to avoid that in the future.

Finally, sir, the debate over the law in the last couple of years has been unique. It has been limited only to talking about changes that would weaken present standards. In my testimony I list a number of changes that might be made in the law in order to strengthen it. The law is not perfect in many respects. Inspection, administrative actions by the FDA, could be substantially improved. I hope as you go through this process that you will seriously consider looking at those areas in which the law might be strengthened.

Thank you.

[The prepared statement of Mrs. Foreman follows:]

STATEMENT OF CAROL TUCKER FOREMAN, PRESIDENT, FOREMAN ASSOCIATES, REPRESENTING CONSUMER FEDERATION OF AMERICA, BEFORE THE COMMITTEE ON LABOR AND HUMAN RESOURCES, U. S. SENATE, JUNE 10, 1983

I am Carol Tucker Foreman, President of Foreman Associates. I serve as an adviser on food and nutrition issues to the Consumer Federation of America and I am here today at the request of CFA to represent them at this hearing. Consumer Federation of America is the nation's largest consumer organization. It is composed of 200 national, state and local consumer, senior citizen, labor, farm, cooperative and rural organizations, which together represent more than 35 million Americans.

Although I am part of a consumer panel, I have also had the experience of attempting to administer some of the nation's food safety laws. From 1977-81, I served as Assistant Secretary of Agriculture for Food and Consumer Services. My responsibilities included the Meat Inspection Act and the Poultry Products Inspection Act. It was during my tenure at USDA that concern was raised about the carcinogenicity of nitrite and appropriate action under the law had to be considered. The public and a substantial portion of the Congress believed then and continue to believe that the challenge to continued use of nitrites arose because of the Delaney Clause. In fact, the most common use of nitrite is in processed meat products and is regulated not under the Delaney Clause of the Food, Drug & Cosmetic Act but under section 601(m) of the Meat Inspection Act, which states that meat is adulterated if it bears any added poisonous or deleterious substance which may render it injurious to health. This general safety standard is common to the Food & Drug Act, the Meat Inspection Act and the Poultry Products Inspection Act.

Nitrite was just the latest chapter in a continuing debate over how the nation's food safety laws should deal with cancer-causing substances. Congressional attention usually has focused on that debate during one of the periodic crises that have arisen over continued use of a carcinogenic substance. Such times are not conducive to the deliberate consideration the issue deserves. These hearings come at a time of relative calm. The exception to the ban on saccharin has recently been renewed. I am not aware of any current study that jeopardizes continued approval of any other widely used substance. There is no legislation pending before the Congress. This set of hearings, focusing on the desirability of making changes in the safety standard and Delaney Clause of the present Food and Drug Act, permitting consideration of benefits in food safety decision making and requiring independent expert review of scientific information may mark the beginning of a rational dialogue on what the nation's food safety laws should look like in the years ahead.

I was pleased that the Committee's letter asked for "comments on the adequacy of FDA's legal authority to assure the safety of the food supply." I intend to address that request in some detail. Although the Committee did not request comments on the Meat & Poultry Inspection Acts and indeed does not have jurisdiction over those laws, I am sure that you are aware of the need for some symmetry in the approach to food safety and will be interested in comments on those laws as well.

Mr. Chairman, I went into the government critical of the safety of the nation's food supply. While I still believe there are serious problems that must be addressed, especially in the area of chemical contamination, I am persuaded that no other nation matches the safety, quality and variety of America's food supply.

This is due in no small part to the soundness of the basic goals and concepts of the food safety laws enacted 77 years ago. The first Meat Inspection Act stated, "it is essential in the public interest that the health and welfare of consumers be protected by assuring that meat and meat food products distributed to them are wholesome, not adulterated and properly marked and packaged." Both the Food, Drug & Cosmetic Act and the Meat Inspection Act adopted at the turn of the century stated that a product is adulterated "if it bears or contains any poisonous or deleterious substance which may render it injurious to health."

From the beginning, the laws have been firm, tough, rigid. They are blatantly biased in favor of the public and the public's health. From the beginning, they have set an exacting standard for the food industry, and each time the Congress has amended the laws, it has been to strengthen the standard. Congress has applied the most rigid standards to food additives because consumers may not be presumed to know of their presence in food, because they serve no essential nutritional purpose and because substitutes are almost always available.

Despite this bias in favor of public health, or perhaps because of it, we have an abundance of safe and nutritious food. It is hard to argue that these laws have impaired either the public's health or the food industry's wealth.

The public does care what happens to the food supply and is perhaps less sanguine about its safety than you or I. In a recent poll conducted by the Food Marketing Institute, respondents were asked about the content of their food and what concerned them most about it. The most frequently mentioned concern was chemical food additives (e.g., flavoring, MSG, steroids). "No preservatives;" and "no harmful ingredients, nothing that causes illness or cancer" were other specific concerns mentioned. All of these items were of greater concern than calories. In this poll and others, consumers respond that it is the government's role to insure food safety and that government should do more not less to assure the safety of the food supply.

Changes in the Delaney clause or the general safety provisions of the Food, Drug & Cosmetic Act or the Meat and Poultry Inspection Acts to make them less exacting will almost certainly raise questions in the mind of the public about whether the food supply will be as safe next year as it is this year. Congress, the Administration, and the food industry should carefully weigh whether the benefits they expect from weakening the standards are worth some diminished confidence in the food supply.

CHANGING THE SAFETY STANDARD AND DELANEY CLAUSE

The present law is more rational and appropriate than its detractors claim. First, the Delaney clause does not require the FDA to ban an additive where any test shows the additive to be a carcinogen. In fact, the FDA is given a great deal of latitude in determining whether a substance is a carcinogen. The Secretary of HHS may determine what tests are appropriate and set the level of evidence necessary to establish that a substance causes cancer. In the saccharin case, the FDA did not act on the study it commissioned, and which indicated carcinogenicity, but awaited results of additional studies. In the nitrite case, the FDA was able to have the Newberne study subjected to intensive slide-by-slide review and to determine, based on that review, that no action was necessary.

Second, the U.S Court of Appeals for the District of Columbia ruled in the Monsanto case that de minimus amounts of packaging materials that migrate into food are not food additives within the meaning of Delaney and do not have to be prohibited if allowing the product to remain on the market clearly presents no public health or safety concerns.

However, the law is rigid in other respects. There is a zero-risk standard. Cancer causing substances must be banned regardless of how weak, regardless of how low the risk. As testing grows more and more sensitive, low levels of cancer causing substances may be found in a number of additives and foods where they are not now detectable. Some people argue that the zero-risk standard creates unreasonable fears in the public, overtaxes the government's resources checking out insignificant problems, sometimes makes the government look foolish because the standard is applied to food and not to other substances, and squelches innovation in the food system.

It is true that we've had some carcinogen-of-the-week scares in recent years as the media report on new research. FDA and USDA have generally been able to handle these in a way that reassures the public.

It is true that sometimes the strictness of the safety standard for food is hard to explain. It takes more than a few words to explain why the government won't allow the sale of bacon that has more than 5 parts per billion of nitrosamines, but does nothing about cigarettes. However, citizens generally believe government should be tougher on cigarettes, not less demanding on food safety.

Hearing food industry arguments, your constituents may think the law is just plain asinine. On the other hand, your constituents want to be safe. They generally agree with food safety policies when they are explained and they would unquestionably look with disfavor on the government that hadn't removed nitrosamines if it turned out they were responsible for cancer in their family.

The problem of limiting technological innovation is an important one. I might be persuaded that it is a reason for change in the zero-risk standard. However, I need more information. Since passage of the Delaney Clause in 1958, very few substances have been removed from the market. None of them seem to have been essential to the food system.

Perhaps the food industry or the FDA should provide an explanation of what we have been denied by the loss of these substances. What foods are not now available that would have been available, what nutritional value has been lost, what safety protection has been denied?

I think it would also be worthwhile to have a list of food additives that were never marketed as a result of the Delaney Clause and an assessment of their value to the public. Perhaps most importantly, we should have a list of substances that are now threatened. Black pepper is mentioned sometimes. However, tests don't seem to make action against it necessary and there are substitutes for it. At least one test has indicated that Vitamin D is a carcinogen. Once again, other tests have not corroborated and FDA hasn't acted. If the data did show that Vitamin D is a carcinogen and that not allowing its addition to foods would jeopardized nutritional well being, a change in the law to remedy that problem should be considered.

Before Congress agrees to rewrite the law, Congress ought to have detailed information on the scope of the problem. If there are a large number of substances that may be found to be carcinogenic, essential to health and without substitutes, perhaps a sweeping change is needed. On the other hand, if there are just one or two or four that meet those requirements, perhaps it would be best to handle the problem with specific exceptions to the law as it is now written.

The specific exemption solution was used to keep saccharin on the market and was proposed when it appeared that nitrite was threatened. Saccharin is a carcinogen. The soft drink industry is heavily dependent on its use. The public wants sugar-free drinks. Congress heard the arguments and granted an exemption. The debate and decision were painful for the industry, the FDA and the Congress. It served the public well. Saccharin is on the market but surely the vast majority of people who use it do so knowing that some risk is involved.

Finally, some witnesses have argued that we must change the law because we will some day be able to determine that some substances that cause cancer in animals do not have the same effect on humans or that there are levels below which some carcinogens do not cause cancer in humans. It would be easier to suggest changes in the law if those things were known now. They are not and risk assessment, though developing rapidly, is still not an exact science.

I am not persuaded that it is necessary to change the law at this time nor that risk assessment is advanced enough to be relied upon to protect the public. Consumer Federation opposes any change that would reduce public protection. However, if

Congress feels it must act, certain steps would make abandonment of zero-risk less troublesome. First, Congress should accept nothing more than a negligible risk from food additives. Second, Congress should assume responsibility for defining the term "negligible", for setting the new risk standard precisely. Bills introduced since 1981 have assigned standard setting to scientific panels or to the FDA. That is convenient for Congress, but it is not good law. The assessment of risk from a given substance is a scientific process. Scientists can do it. The determination of how much risk is acceptable is a political question. It requires a choice between competing groups within society. It is a choice that must be made by Congress.

You may find a one in one million lifetime chance of cancer appropriate to balance the interests of using a product against the interests of public health protection. You may find that a one in ten million lifetime chance is better. But you must set the numbers.

There is another reason why Congress rather than a scientific panel or FDA bureaucrats should set the standard for negligible risk. Surely you know that if either of those groups establish acceptable risk and a given substance fails to meet it, advocates for that substance will be at your door charging the standard is inappropriate and the decision makers biased and a Congressional override of their position justified.

Finally, a Congressionally mandated standard seems especially important because any change in the law will represent a weakening of the present zero-risk standard. Agencies do take their cues from Congress. It will not go unnoticed that this change was sought by the affected industry. Unless Congress is very specific about what it wants and expects, it may find that FDA and USDA have perceived the change to be a signal to go slow and go easy. The result of such a change might lead to a period of dangerous inaction and a threat to public health.

BALANCING RISKS AND BENEFITS

Let me turn now to the question of balancing risks against benefits. When there is a direct health benefit to be gained from use of a cancer causing substance and no acceptable substitute is immediately available, the law could provide for some continued use on at least a limited basis.

The use of nitrite in processed meats is the only case I know where that balancing benefit might have been necessary. Nitrite is used in virtually all processed meat products. In addition to its coloring and taste properties, it is an extremely effective preservative, used to prevent the growth of clostridium botulisum. Processed meats can be protected against this deadly organism in other ways, but no other way has ever been used by an industry that is extremely diverse in size and technological sophistication. All meat is not processed in laboratory clean conditions. Inspection is not perfect. Botulism is deadly. My colleagues here at the table tend not to agree with me, but I was and am persuaded that removing nitrite from meats without an immediately available substitute that could be easily used would have created a serious health risk.

It would seem worthwhile to allow balancing of health risks and benefits if the health benefit can be demonstrated, the substance has been on the market for some time, and there is no practicable substitute. I cannot think of any reason to balance economic benefits against health risks. The equation is clearly unbalanced. Benefits accrue to one group, risks accrue to another.

PHASING OUT SUBSTANCES

In the nitrite case, continued use of a carcinogenic substance could have been limited by the development of either alternative processing and distribution systems or other preservatives. We needed to give the food industry time to act and an incentive to act quickly. Legislative authority for a phase out could have provided that. The assurance that government would proceed in a phased fashion might have reduced industry opposition to action against nitrite and possibly speeded its removal from the market place. If phase-out provisions are added to the law, they should be drafted in a fashion that generates an incentive for faster rather than slower action. One period of three or four years should be sufficient to create pressure both on industry and government to search for alternatives. If vigorous efforts to find substitutes fail, the industry could appeal to Congress for legislative authority for an additional period. An automatic extension written into the law will be tantamount to adding that time to the process of removal in every case.

During the phase-out period, the Secretary of HHS should have authority to take actions that will reduce the health risk as much as possible. He should be able to require labeling products in which the substance is used, to establish classes of food in which it is used and set phase-out times appropriate to each class, and to reduce the quantity of the substance used in each class to the minimum required for its health benefit.

I endorse risk balancing and phase out with some reservations. Once again, there is the problem that in the history of the laws in question, no substance meets the qualifications that I would require for balancing and phase out. Nitrite has not been shown to be a carcinogen and the health benefits of saccharin are questionable. Unless there is hard evidence that a number of substances may fit the pattern in the future, case by case action may be preferable.

REQUIRING PEER REVIEW

A technologically and scientifically complex world creates a yearning for certainty. Each time there has been a debate over the food safety laws, with government acting or failing to act and one group or another outraged by the result, the suggestion arises that the decisions made were political rather than scientific. The next step is usually a proposal for a science court or advisory body of scientists from outside the government who would gather all of the scientific evidence and render an opinion from on high, an opinion based solely on data, free from regulatory and even human biases.

Certainly decisions with potential for great impact on the public health or the economic condition of the food industry should have the benefit of the best data provided by the most knowledgeable scientists. If an outside group adds to the body of knowledge, it can be useful. However, a peer review group that will seriously effect decision making of the FDA should be established by and answerable to the Secretary of Health and Human Services. He should have discretion over which critical scientific issues should be submitted for peer review. It may be desirable to exclude FDA scientists from the Committee, but it seems unwise to exclude representatives from NIH. On the other hand, it is fair to ask whether membership should be denied to any scientist who is in the employ of or receives grants from a corporation whose economic interests are affected by the outcome of a particular issue. Finally, let me raise a very practical point with regard to referring issues to an august, outside group. Scientists of such qualification have fulltime employment outside the government. They are not people with a great deal of free time. It is naive to assume that they could drop everything and come to Washington to debate an issue at great length on a regular basis. As with all such committees, a great deal of the work would be performed by staff and the final results will bear the marks of that staff perhaps more than the members of the committee.

The ultimate problem with a peer review committee is that it must be limited to its area of expertise, science. As in the definition of acceptable risk, the final choice on policy must be made not by outside scientists but by those whom the people have entrusted with policymaking power in the government.

STRENGTHENING FOOD SAFETY LAWS

The debate over the food safety laws in the last two years has been unique. Not one word has been said about strengthening the laws. There are weaknesses in the law and Congress should consider taking steps to remedy them.

Food constituents that cause irreversible effects other than cancer -- including birth defects and gene mutations -- should be regulated as strictly as carcinogens.

The different treatment of direct additives, foods generally recognized as safe, color additives, and prior sanctioned substances has no scientific justification. There should be one constituents policy governing all. Food additives currently in use that are found to be carcinogenic might, in some cases, be authorized for sale as separate food products in a method similar to that of over-the-counter drugs.

In 1977, the FDA proposed to eliminate the use of subtherapeutic doses of penicillin and tetracycline in animal feed. An Appropriations rider for FY 1978 and subsequent years prohibited that action and ordred an extensive study on the threat to human use of these important drugs. The study, completed last year, is not reassuring. It states that it cannot be ascertained that this use does not create a threat of human health problems. Until no harm can be demonstrated, Congress should act to prohibit subtherapeutic doses of penicillin and tetracycline in animal feed.

Although there has been substantial debate over the cancer clauses since 1981, no attention has been given to the need to improve the basic enforcement powers of FDA. Congress should act to give the agency authority to:

- require registration of food processors;
- administratively detain food products that may be adulterated or misbranded;
- require notification of the FDA by a food processor that adulterated food has left his premises or that he has instituted a recall because he has reason to believe food may be adulterated or misbranded;
- require processors to institute a food coding system in order to implement and monitor recalls of food;
- require each processor to make and maintain records of the distribution of foods through any establishment owned or operated by the processor and provide to inspectors access to and the ability to copy and verify any records bearing or whether food manufactured, processed, packed or held in the facility inspected is adulterated or misbranded;

- require notification of the FDA by a food processor that adulterated food has left his premises or that he has instituted a recall because he has reason to believe food may be adulterated or misbranded;
- require processors to institute a food coding system in order to implement and monitor recalls of food;
- require each processor to make and maintain records of the distribution of foods through any establishment owned or operated by the processor and provide to inspectors access to and the ability to copy and verify any records bearing or whether food manufactured, processed, packed or held in the facility inspected is adulterated or misbranded;

- assess civil penalties.

These recommendations for providing very basic regulatory tools to FDA have been made a number of times. Most of the powers were granted to USDA years ago. It is hard to justify a reason for the agency that inspects 10% of the nation's food supply having more authority to carry out its functions than the agency that inspects the other 90% of the food supply.

In 1980, the FDA, USDA and FTC recommended changes in food labeling that would provide more and clearer information to consumers on ingredients and nutrition and contents of standardized foods. This Administration has dropped all efforts toward enactment of those recommendations. The problems, however, still exist and some action should be taken.

Last year Congress debated, but did not enact, legislation to require sodium labeling. Such labeling is a very important tool to the millions of Americans who are on salt restricted diets. FDA has instituted a voluntary program. It has not met with wide success. USDA has refused even to take that basic step. Congress should now step in and make such labeling mandatory.

This Committee does not have jurisdiction over the Meat Inspection Act and the Poultry Products Inspection Act. However, to accomplish the goals desired by the food industry will require changes in the general safety standards of those acts. Other amendments to those acts would serve the public well. Chemical contamination of meat and poultry products is a serious problem for food processors as well as consumers. USDA inspectors violate the law by approving as safe, meat and poultry products that contain harmful chemical residues. USDA needs additional appropriations for research on better testing methods and to conduct more sampling. In addition, Congress should pass legislation introduced in 1980 that would require the USDA to establish an animal identification system and quarantine program. This authority is the only way, given the inadequacy of present testing methods, to reduce the level of chemical contamination of meat and poultry products by tracting violations back to the source.

These are just a few examples of issues that Congress must grapple with as it reviews the food safety laws. Admittedly, the visits to your offices are by representatives of affected industries who tell you that the public cannot expect to live in a zero risk society. They want to see the food safety laws changed, not to improve public health protection, but to make their own lives easier and their businesses more profitable. There is no zero-risk guarantee for business either. We live in a rapidly changing world and new science may uncover unpleasant facts about substances in use for many years. The answer must almost always be to withdraw the substance, not tell the public to live with it.

There is nothing sacred in the food safety laws as they exist today. They should be subject to modernization and improvement. But Congress and the food industry should be wary of proposals that substantially reduce public protection. If enacted, they will tend to undermine public confidence in the food supply and may lead to circumstances that would create a backlash and even more rigid laws. A tough but consistent law would seem to benefit the industry more than one which swings with the pendulum of political power.

The **Chairman**. Thank you, Mrs. Foreman. We appreciate your keeping within the time limit, too. I appreciate your testimony.

Ms. Haas?

STATEMENT OF ELLEN HAAS, EXECUTIVE DIRECTOR, PUBLIC VOICE FOR FOOD AND HEALTH POLICY, WASHINGTON, D.C.

Ms. **Haas**. Thank you, Chairman Hatch, Senator Quayle. It is a delight to be here representing Public Voice for Food and Health Policy.

Along with me are the groups that are part of the Coalition for Safe Foods. We who are here today are strongly united in the belief that the consumer protections in the Federal food safety laws must be preserved, and especially that the strict requirements for safety and the minimal discretion for Federal regulators as applied to substances which are deliberately added to food must be maintained. We strongly believe that the case has not been made for making any changes in the present food safety laws which would provide for more lenient safety standards or greater agency flexibility in this area, and that the kind of sweeping statutory changes that are currently being discussed are premature and wholly inappropriate.

In this sense, you might say we represent a conservative approach to food safety. We believe in conserving the strong safety protections in the present law and, thus, conserving the Nation's health.

The groups here today are leaders of the Coalition for Safe Food, which includes more than 40 consumer, environmental, labor, and senior citizen organizations. They are joined in their commitment to a strong food safety, and it is demonstrative of the powerful and overriding consumer concern in a food supply that is the safest it can be, not necessarily absolutely risk-free, but free of all unnecessary risks and hazards.

National public opinion reflects this concern as well. In a recent Lou Harris poll that was released just a month ago, it reported that 8 of every 10 consumers polled felt very or closedly described by the statement, "I feel concerned that some ingredients added to processed foods may be harmful or unsafe to eat."

Also, nearly three of every four polled said they avoid buying certain foods because of concern about whether or not they are safe. Changes made today by Congress that would weaken or jeopardize food safety protection will only serve to further shake consumer confidence in the quality of the food supply and provide the public with additional evidence that Congress is not so much concerned with protecting the public health as it is with providing greater regulatory freedom for American industry.

Instead, we feel that the committees responsible for the safety of the food supply should be looking to strengthen protections in our food safety laws in the areas that need to be strengthened and to eliminate unnecessary consumer hazards.

Before suggesting a number of these improvements, I think it is important for just a moment to address an issue that I think is of utmost importance since it has been the center of these hearings. The Delaney clauses have time and again been assailed by many as being inflexible and antiquated and in need of modernization to keep pace with the technological advances. However, we believe they are fundamentally important elements of the Nation's food safety laws which are every bit as valid and necessary as when they were enacted 25 years ago.

While scientists have made great strides in developing techniques to measure the degree of risk from particular chemicals, there is still considerable scientific disagreement as to the accuracy of such techniques. As a demonstration of this disagreement, I would like to submit for the record a paper done by Dr. Samuel Epstein of the University of Illinois and Thomas Smith.

The CHAIRMAN. Without objection, that will go in the record at this point.

Ms. HAAS. Thank you, Mr. Chairman.

[NOTE: In the interest of economy the paper by Dr. Samuel Epstein and Thomas Smith was retained in the files of the committee.]

Ms. HAAS. Instead of spending our energy on devising ways which we can ease the restriction of the Nation's food safety laws, we believe the public would be better served through the consideration of changes which would strengthen these statutes and provide for improved consumer protections in areas where the laws are currently inadequate.

In April of this year Public Voice completed a study of the areas in which the safety of the Nation's food supply needs to be improved, and I would like to submit the report, "A Market Basket of Food Hazards: Critical Gaps in Government Protection," into the record as well.

In addition, I would like to just list those areas that we recommend where improvements should be made in the Federal food safety laws.

One, we believe that Congress should strengthen the authority for regulation of pesticide residues. A recent FDA study group in fact has recognized its ability to carry out this area is impaired and it needs additional authority to detain produce suspected of being adulterated with pesticide residues.

The second area of importance is that there is authority necessary for mandatory inspection for fish products. As fish consumption goes up, we still have a very small percentage of all fish which is inspected because it is a voluntary program.

Three, we believe that there is a need for the providing of additional authority to the Department of Agriculture to take action to limit the marketing of hazardous meat products that contain violative chemical residues. We heard this morning how the agencies feel that they have adequate authority. However, too much of chemical residue laden meat is marketed, and the GAO has made recommendations of ways to strengthen this area. We believe it is essential.

Fourth, there is a need for Congress to provide clear direction to FDA for tolerance setting of unavoidable contaminants such as aflatoxin, a potent cancer-causing mold, and limit the use of the action level setting process which is informal, takes place without any notice and comment.

Fifth, the provisional list of color additives should be terminated. After all, Congress only intended it to last 2½ years. Instead, it is now 20 years since it was started, and it still continues.

Sixth, there is a need for Congress to strengthen and simplify the process of removing carcinogenic, permanently listed color additives.

Last, there is a need for Congress to amend the act to ban the use of penicillin and tetracycline in animal feed, as FDA proposed in 1977.

Finally, we believe that these are the areas that deserve the attention if the committee is truly committed to enhancing the safety of the food supply and that it will not proceed further with changes that are premature and which pose great risk to consumers.

Thank you very much.

[The prepared statement of Ms: Haas follows:]

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Testimony of Ellen Haas
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Before the Labor and Human Resources Committee
United States Senate
June 10, 1983

A Conservative Approach to Food Safety

Chairman Hatch, my name is Ellen Haas and I am the Executive Director of Public Voice for Food and Health Policy, a non-profit consumer research, education and advocacy organization with expertise in the areas of food, nutrition, and agriculture policy. We are pleased to be able to provide to you and the Committee our thoughts on federal food safety protections, an area which is all important to American consumers.

The groups which are represented here today are strongly united in the belief that the consumer protections in the federal food safety laws must be preserved and especially that the strict requirements for safety, and the minimal discretion for federal regulators, as applied to substances which are deliberately added to food, must be maintained. We strongly believe that the case has not been made for making any changes in the present food safety laws which would provide for more lenient safety standards or greater agency flexibility in this area, and that the kind of sweeping statutory changes that are currently being discussed are premature and wholly inappropriate.

In this sense we believe we represent a conservative approach to food safety law -- we stand for conserving the status quo, conserving the strong safety protections in the present law, and conserving the health of the American people.

The groups here today are also the leaders of the

Coalition for Safe Food, a group of nearly 40 national, state and local organizations committed to maintaining strong food safety laws. This coalition was formed in 1981 and we are presently expanding the coalition to include representatives in every state in the union.

The existence of this coalition, and its commitment to strong food safety, is demonstrative of the powerful and overriding consumer concern in a food supply that is as safe as it can be made -- not necessarily absolutely risk free, but free of all unnecessary risk and hazard. These are principles upon which the present law is based and it is this foundation which must be preserved.

This concern, moreover, is not limited to just the consumer groups represented at this table or in the Coalition for Safe Food. It spans the entire U.S. population. In fact, in a nationwide consumer survey conducted in 1983 by Lou Harris and Associates, eight of every ten consumers feel "very" or "closely" described by the statement

> "I feel concerned that some ingredients added to processed foods may be harmful or unsafe to eat."

In addition, nearly three of every four consumers avoid buying certain foods because of concern about whether or not they are safe. One other interesting statistic is that the two population sub-groups that are most concerned about food safety are urban dwellers (71 percent) and Westerners (69 percent).

Clearly, the interest in and concern about the safety of the food supply is deep-felt and widespread. Moreover, it serves no interest to attempt to make changes in food safety protections when there is no practical need for doing so and when public concern about government protection of the public health in all areas is great and growing steadily. Changes made today that would weaken or jeopardize food safety protections will only serve to further shake consumer confidence in the quality of the food supply, cause disturbances in food purchasing patterns, and provide the public with additional evidence that the government in Washington is not so much concerned with protecting the public health as it is with providing greater regulatory freedom for American industry.

Instead, we feel that this Committee should be looking to strengthen consumer protections in our food safety laws, to focus its attention on those areas of the Food, Drug and Cosmetic Act and the Meat and Poultry Inspection Acts that need to be strengthened and improved to eliminate unnecessary consumer hazards.

Before suggesting such improvements, however, I want to discuss one of the more important issues on which this Committee has focused in the past and which will likely be addressed in any bill which emanates as a result of these hearings.

The provisions of the Food, Drug and Cosmetic Act which prohibit the use of any direct or indirect food or color additive that is shown, through appropriate tests, to cause cancer in man or animals have been assailed by many as being inflexible and antiquated and in need of modernization to keep pace with the technological advances. We firmly believe, however, that the Delaney clauses are fundamentally important elements of the nation's food safety laws which are every bit as valid and necessary as when they were enacted 25 years ago and which provide important health protections to consumers.

The Delaney clauses have been accused of injecting a "zero-risk" concept into the federal food safety laws yet by and large this is not the case. For the vast majority of foods and food ingredients the strict provisions of the Delaney clauses do not apply. For raw agricultural commodities and natural contaminants therein, the safety standard applicable allows the agency to exercise substantial discretion in regulating hazards, including carcinogens. By this standard, naturally-occurring substances in food do not render it adulterated unless such substances "ordinarily" render the food injurious to health. At least with respect to natural contaminants, such as aflatoxin in grains and legumes, the FDA is empowered to set tolerance levels which limit but do not prohibit such hazardous substances from the food supply.

Similar flexibility is inherent in the authority of the FDA to regulate hazardous pesticide residues present on fresh foods or in processed products as well as residues of animal drugs in meat. Even for substances the lay public would consider food additives but which enjoy a usage which predates 1958 or which, on the basis of scientific evidence or history of usage, are Generally Recognized as Safe (GRAS), the restrictions of the Delaney clauses do not apply.

In addition, for health hazards other than cancer, even direct and indirect food and color additives are not banned automatically; the FDA has the authority to consider the full range of evidence on hazards and functionality in deciding whether to remove an additive from the market.

Finally, even with respect to indirect additives the FDA has been provided with flexibility in regulating carcinogens which migrate into food products. This flexibility, laid down by the U.S. Court of Appeals for the District of Columbia Circuit in Monsanto v. Kennedy, 613F.2d947 (1979) allows the FDA some amount of administrative discretion in dealing with de minimis situations regarding indirect additives when the agency determines that such situations clearly present no public health or safety concerns.

Thus it is only for the very narrow category of direct food and color additives and only for the one public health hazard of cancer that the strict prohibitions of the Delaney clauses apply. In these cases, moreover, the restrictive safety standards -- which prohibit the use of any amount of a substance if it is shown to be carcinogenic -- are still very much in line with the current state of the science of cancer risk analysis and are still necessary to protect the public health.

When the Congress determined, in 1958, to set down stricter standards in the food safety laws for carcinogens as direct food additives, it did so because cancer was a major disease, growing in importance in America, incurable and little understood in terms of when it would strike and why. A national policy was emerging to do everything possible to conquer this dread disease and the Congress determined that the American public should not have to incur any increased risk of cancer from substances which are only in the food supply because of their direct addition by food manufacturers. And since consumers are exposed to so many carcinogens from natural food and environmental sources, this strict prohibition at least eliminated one controllable source of exposure.

Both these policy reasons for the Delaney clauses exist today.

While our scientists have made great strides in developing techniques to measure the degree of risk from particular chemicals, there is still considerable disagreement in the scientific community as to the accuracy of such techniques in general and as to which specific technique in particular is the most appropriate. As a demonstration of this disagreement I would like to submit for the record a paper that was done by Dr. Samuel Epstein of the University of Illinois, with the assistance of Thomas B. Smith, now the Director of Government Affairs for Public Voice, for the 4th National Food Policy Conference: Focus on Food Safety, in 1981. It was at this conference, I might add, that Dr. Sanford Miller, Director of the FDA Bureau of Foods, likened the process of risk assessment to "black art". Generally, the paper discusses the lack of refinement of risk assessment procedures today and argues that food safety law modifications based on formal risk assessment tools are premature at this time.

With respect to the second point, there is still no good reason to permit food manufacturers to use chemicals that cause cancer as food additives. Such an additional cancer risk is unnecessary because such substances only gain entry to the food supply by their direct addition by food processors and because in virtually every instance such chemicals have safe substitutes. Many chemicals are available to color, flavor and preserve food; if one is hazardous and requires banning, there is always another to take its place.

Of course there is always the exception. But in the modern history of the food safety laws there has been only one instance where an exception has been required -- saccharin. And in that case, after the FDA determined that the substance was carcinogenic and could no longer be used as a food additive, the Congress intervened to keep saccharin on the market in response to what it perceived was wide public demand for the product. This decision was not based on risk assessment, a risk-benefit computation, or even a risk-risk analysis. Instead, the Congress acted the way it did due to public demand for saccharin -- an element in food safety decision-making that the FDA is not prepared to analyse and which is properly evaluated only through the political process. Modifying the Food, Drug and Cosmetic Act to empower the FDA to make food safety decisions based on popular demand -- in effect rewriting the laws to conform to this one exception -- would vest in the agency powers which go far beyond its area of expertise and would politicize the decisions of an agency which should remain grounded in science, not public opinion.

Another example which is often cited as evidence of the inflexibility of the food safety laws is nitrite. If the additive had been found to be cancer-causing and had required banning, the argument goes, a significant health protection would have been lost. Setting aside the dispute over the need for nitrite as a health protection for botulism, the question remains hypothetical, as the substance itself is not now considered a carcinogen. As a mere hypothetical, we believe the arguments are not strong enough to modify the food safety laws on its basis.

As an academic question, allowing for a risk-risk analysis in food safety decision-making (as would be required for nitrite) has some appeal because such a process would clearly fall more in line with the range of FDA expertise as a scientific agency. In addition, a showing that a particular additive confers major and irreplaceable health benefits on the public does rebut one of the two important presumptions which underlie the food additives amendments -- that no carcinogenic additives should be used because there are generally safe substitutes. Yet because this question is wholly academic at this time, we believe there is currently no reason to modify the food safety laws to provide the FDA with this authority. After all, such authority could be abused through findings of public need for an additive, when none actually existed, merely to keep a particular additive on the market. Of course, this is not to say that an additive which was found to prevent a major health risk would automatically be removed from the market; as with saccharin, such an additive could always be treated as an exception, and the FDA could even recommend to Congress how the particular exception should be addressed. If, over time, we found that exceptions were becoming routine, then could we consider making provision in the laws to allow for regular risk-risk based decisions for food additives.

Mr. Chairman, instead of spending our energy on devising ways through which we can ease the restrictions of the nation's food safety laws we believe the public would be better served through the consideration of changes which would strengthen these statutes and provide for improved consumer protections in areas where the laws are currently inadequate.

In April Public Voice completed a study of the areas in which the safety of the nation's food supply needs to be improved and I would like to submit a copy of this study for the record.[1] Based on this study we would like to recommend the following improvements in federal food safety laws:

* Mandatory Inspection of Fish Products: Because only a small percentage of all fish is inspected through a voluntary program of the National Marine Fisheries Service and because the FDA inspection program for fish results in inspector visits to plants only on very rare occasions, a program of more comprehensive inspection, mandatory for all fish processing plants, must be adopted. In addition to problems of sanitation and shelf-life, fish products have recently been implicated in problems relating to viral disease, pathogenic parasites and serious chemical contamination (dioxin).

* Strengthened Pesticide Residue Authority: The use of pesticides in food production today is extensive and many pesticides must be limited in their application for purposes of common safety. Other pesticides are deemed so hazardous, or

produce by-products that are so lethal, that they may not be used at all. While the Environmental Protection Agency is charged with the responsibility of setting tolerances, it is the job of the FDA to actually monitor produce for violative levels and illegal residues, prevent the sale of such adulterated products, and take enforcement action against the producers who are responsible.

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[1] "A Market Basket of Food Hazards: Critical Gaps In Government," April, 1983.

Yet the FDA itself has recognized that its ability to carry out this responsibility is severely impaired and that it needs additional authority under the Food, Drug and Cosmetic Act to adequately protect the public.

In particular, a 1979 FDA study group recommended that the Act be amended to give the FDA the authority for (1) administrative detention of commodities suspected of containing illegal chemical residues and (2) the assessment of civil penalties against those misusing pesticides. In addition, the public health could be more adequately protected if the agency were given a broader statutory definition of "interstate commerce" for purposes of taking regulatory action.

While the Act now authorizes the FDA to seize food or feed products adulterated with illegal pesticide residues, to pursue injunctive relief against those selling into interstate commerce produce containing illegal pesticide residues, and to seek criminal penalties against these interests, these tools are generally inadequate for the awesome task the FDA must perform. Seizures are only used in rare occasions because (1) the commodity did not move in interstate commerce, (2) voluntary or state-initiated destruction of the food took place, or (3) as in a "substantial number" of instances, the produce had moved further into commerce and could not be traced or had already been consumed.

Injunctive relief is even less useful in these instances because it is used prospectively only -- to stop further shipment of an adulterated product -- and thus has no value when a crop has been completely harvested and marketed or residue levels on a particular farm are no longer at excessive levels. In no case does it prevent the sale of produce which _is_ known to be adulterated.

Criminal prosecution is similarly inadequate to protect consumers because of the enormous time involved -- often several years of FDA investigatory work.

Thus the additional authority would serve to allow the FDA to detain produce suspected of being adulterated with pesticide residues so that the agency could have enough time to assure its safety before releasing it into commerce. Present enforcement tools provide no economic incentive to use pesticides properly; if individual shipments would be banned from the market upon a finding of violative residues such an incentive would be implanted, consumer protections would be enhanced, and the number of residue violations would necessarily decline.

According to the FDA Study Group,

> Administrative detention authority is available to FDA for controlling imported food and feed commodities and for controlling the movement of suspected adulterated meat, poultry, and eggs in domestic commerce outside USDA official establishments. Therefore, the absence of such authority for other foods and animal feed in domestic commerce represents a deficiency in the Agency's control authorities.[1]

Authority for the assessment of civil penalties would also be of great use, in light of the time-consuming nature of pursuing criminal penalties and the reluctance of the FDA to seek such penalties for one or a limited number of confirmed violations by one interest. According to the Study Group, "(a)ssessing civil penalties (fines) would have a punitive effect and would indicate the agency's refusal to tolerate pesticide violations. This in turn should have a deterrent effect on other pesticide applicators, growers and manufacturers."[2]

We believe any legislation modifying this nation's food safety laws must contain these improvements in order to better protect the public from the growing hazards of pesticide use.

* Chemical Residues in Meat: Problems analogous to those described in the previous section of this testimony are common

to meat products and in 1979, extensive reports by the General Accounting Office, the Department of Agriculture itself, and the Booz, Allen and Hamilton consulting firm recommended that the USDA be provided with additional authority to protect the public health. Thus we believe the Federal Meat Inspection Act should be amended by:

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[1] "FDA Monitoring Programs For Pesticide and Industrial Chemical Residues in Food," Study Group on FDA Residue Programs, June, 1979, p.67.

[2] *Id.*

(1) Providing USDA with authority to quarantine animals to prevent the marketing of additional animals by a violative grower until action to correct the violation problem has been taken;

(2) Authorizing the USDA to require growers to place identification tags on animals before they are sent to an auction house or slaughterhouse;

(3) Authorizing the USDA and FDA to levy civil penalties on processors when problems of pesticides and other chemical contaminants are discovered.

* Tolerances and Action Levels for Contaminants: The Food, Drug and Cosmetic Act now authorizes the FDA to set tolerance levels for "unavoidable" contaminants of food (e.g. aflatoxin) in order to protect the public health. Yet in the case of aflatoxin the FDA has never published a tolerance level and instead relies on informal action levels, which are set without the benefit of a notice and comment rulemaking. These action levels are considered to be excessive by many (including the last Republican Administration which proposed to lower the action level for one important product -- peanuts) and the FDA has repeatedly allowed exemptions from these action levels of aflatoxin exposure than those ordinarily permitted, again without any notice and comment.

For these reasons we believe that Congress should specifically instruct the FDA to set formal tolerance levels for aflatoxin. Section 406 of the Act should be amended to permit the use of action levels only in those instances where an exposure level lower than that permitted through the tolerance is required to protect the public health and that such an action level should be effective immediately upon announcement. If exception is to be made from either a tolerance or action level, the formal rulemaking procedures set down under 21 U.S.C. §701(e) must be followed.

* Provisional List of Color Additives: Established in 1960, the provisional list of color additives was conceived as a short (two- or three-year) grace period for manufacturers of color additives which would allow the continued use of certain color additives while safety testing was underway. This short grace period has been extended repeatedly, with the result that consumers have needlessly been exposed to color additives known to be hazardous or not shown to be safe. Nearly one dozen color additives remain on the provisional list today; its immediate termination would provide a significant health benefit for the public. (Carcinogenic additives on the list include FD&C Red No.3.)

* Permanent List of Color Additives: Removing an additive from the permanent list of such substances requires enormously cumbersome administrative procedures which prolong public exposure to a permanently listed color additive once it has been found to be hazardous. The Act should be amended to allow for the expedited removal of such additives.

* Human Drugs Used on Meat Animals: In 1977 the FDA proposed to withdraw all feed uses of two key human antibiotics --penicillin and tetracyclines. The agency has been stymied in its effort to protect the effectiveness of these critical drugs in treating human disease by both the chemical industry and the Congress. The FDA under the present Administration has moved in the opposite direction -- to allow the use of new and different feed formulations containing these antibacterials. The Congress should amend the Act to ban the use of penicillin and tetracycline in animal feed as the FDA proposed in 1977.

Mr. Chairman, these modifications in the Act are greatly needed if the federal agencies charged with the responsibility of protecting the public health are to be able to accomplish their mission effectively. If this Committee is truly committed to enhancing the safety of the food supply it will not proceed further with changes that are premature and for which there is no practical need. Instead it will recommend to the Senate that the improvements herein discussed be made in the Act and that the only increase in discretion and authority for the FDA at this time be that necessary to properly enforce the present protective provisions of the Act.

Mr. Chairman, I appreciate the opportunity to present the views of Public Voice on this important subject and am pleased to answer any questions you may have concerning our position.

The CHAIRMAN. Thank you, Ms. Haas.
Mr. Schultz?

STATEMENT OF WILLIAM B. SCHULTZ, ATTORNEY AT LAW, PUBLIC CITIZEN LITIGATION GROUP, WASHINGTON, D.C.

Mr. SCHULTZ. Thank you, Senator Hatch.

In addition to my prepared testimony, I have also submitted comments on S. 1442 as well as comments on the administration's proposals, and I would ask that those be included in the record.

The CHAIRMAN. Without objection, we will place them in the record immediately following your written statement.

Mr. SCHULTZ. Thank you.

I would like to say a few words about the question of the definition of safe because I regard that as probably the most fundamental issue.

As you have heard many times, the legislative history does contain a definition of safe, which is reasonable certainty of no harm, and I think it would be very difficult for anyone to object to codifying the legislative definition that the FDA has been using for 20 years, although I do not know that such an amendment would be necessary.

The testimony you have heard today essentially creates a strawman. The administration is arguing that the standard is, in fact, a zero risk standard, and I want to say to you that that is simply not true. There is no support for that argument in the definition that Congress adopted, and there is no support for that claim in the practice of the FDA over the past 20 years. It is not a zero risk standard, I do not think you have been given any examples which would show that it is.

Dr. Hayes made the statement today that a zero-risk standard is not an achievable or a desirable goal. Well, I do not know if it is an achievable goal, but I certainly think it is a desirable goal. I guess I think that the current act tries to get as close to that kind of standard as we can and still be realistic, and I think that is the sort of approach that all of us would support.

There is one place where the act adopts a zero risk standard. It is not in the definition of safe, but it is in the Delaney clause, and I would like to now turn to that issue.

There are essentially three arguments that are made by those who support repealing the Delaney clause. The first is that the Delaney clause does not allow the FDA sufficient scientific discretion. As the argument goes, the Delaney clause would require the FDA to ban an additive where a single animal test shows that the substance is a carcinogen, even if that animal study is flawed. That argument simply is not correct.

First of all, the language of the Delaney clause refers to tests which are appropriate for the evaluation of the safety of food additives, so the discretion is built in to the clause itself.

Second, the FDA has administered the Delaney clause in a way that shows that it recognizes it has this discretion. For example, in the case of saccharin there is an FDA study as far back as 1972 showing that saccharin caused bladder tumors. There are also several subsequent studies, and yet the agency awaited additional studies before it made the decision on saccharin, and the current statute gives it this discretion.

The black pepper example is another example of discretion to identify appropriate tests under the statute. As I understand it, there is one skin test that suggests that black pepper is a carcinogen, but the FDA has looked at the evidence presumably and concluded that that is not sufficient under the Delaney clause to show that black pepper is an animal carcinogen. Therefore, it has not moved to ban the substance. It does not need any additional statutory authority to take that position with regard to black pepper.

The second argument is that modern science has made the Delaney clause obsolete because we can now measure minute quantities of substances, such as packaging materials, that can migrate to food. Where those substances are carcinogens, the argument is that the Delaney clause would require a ban of the whole substance. That, I think if you look at the testimony, is really the argument that is made most frequently, and the argument had some merit until 1979 when the D.C. circuit issued the decision in *Monsanto* v. *Kennedy.* That decision states that the FDA has the discretion to exempt a very small amount of a substance that migrates to food from the definition of food additives. If the substance does not qualify as a food additive, then, of course, the Delaney clause does not apply.

Whatever merit that argument might have had before 1979, I don't believe it has any merit today. This is the argument that is made, along with the statement that technology has moved so fast that we can now measure such minute quantities. That is all true, but the D.C. circuit has given the agency ample authority under the statute to deal with the problem.

The third argument is that the scientific assumptions underlying the Delaney clause are no longer valid. In essence, the argument is that whatever the case might have been in 1958, it is no longer appropriate to assume that an animal carcinogen is also likely to be a human carcinogen. My understanding of the science is that this argument is simply not correct today. We may come to a point in the future where we will be able to identify animal carcinogens that are not human carcinogens. If that happens, it will be appropriate to modify the Delaney clause.

However, insofar as I am aware, no one at these hearings has identified a single example of an animal carcinogen that they are willing to say is not a human carcinogen. Until you have those examples, I do not believe it would be appropriate to modify the Delaney clause.

I want to say a word about benefits as well because it has been suggested that the FDA ought to be allowed to take benefits into account when approving food additives.

It is true that the agency takes benefits into account in other situations. For example, in deciding whether to approve a drug, it must decide whether the benefits of that drug outweigh the risks of the drug. Thus, it can approve a drug that is a carcinogen if the benefits of the drug are greater than the risk of cancer.

Food additives, however, are a different matter. In general, they are either interchangeable or unimportant. For example, it matters very little to the consumer whether the manufacturer uses red dye

No. 2 in processed food or some other color of red or no color at all. Similarly, most preservatives are also interchangeable and, therefore, not essential. It is for this reason that Congress 25 years ago decided that consideration of benefits was not necessary or appropriate when deciding whether to approve food additives.

Hearings on the Delaney clause in 1960 offer an educational example of why it is important to be cautious and of just how wrong the experts can sometimes be. The 1960 hearings were the first debates on the Delaney clause. Among the witnesses was Dr. Thomas Carney, a vice president of Eli Lilly Co. The gist of his testimony was that Congress should not adopt the Delaney clause because the assumption that an animal carcinogen is also a human carcinogen was, in his view, incorrect. As an example, to support his testimony, he cited diethylstilbestrol, or DES, which he pointed out had been found to cause cancer in a few species of animals.

However, Dr. Carney argued that this substance had been used in human drugs for more than 20 years, even as of 1960, and that it was so safe that doctors prescribed it to pregnant women in order to prevent miscarriages. He then quoted experts who had concluded that in 1960 DES was safe for humans and that any correlation between DES and human cancer was, in their words, "most probably mythical."

Twenty years later we are much wiser. We know that DES causes a rare form of vaginal and cervical cancer in the daughters of the pregnant women who were prescribed the drug. We also know that 80 percent of those daughters have developed a condition called "adenosis," which is an abnormal vaginal condition. In addition, a significant percentage will have problems during pregnancy, including prematurity, and all of them, as well as DES sons, have a risk of infertility.

It may be true that Dr. Carney did not know in 1960, when he and his company vigorously promoted the use of DES as a drug and as an additive for animal feed, that the product would injure so many people. However, the whole point of the Delaney clause is that, in general, food additives are not particularly important, and, because there is so much we do not know, our laws ought to be designed to require the Federal agencies to err on the side of safety.

For this reason, as well as other reasons, we oppose the efforts to weaken the food safety laws. However, we would favor strengthening them by eliminating the prior sanction provision, the provisional list, and the other examples that have been given today.

I would like to note that Donald Kennedy, when he was Commissioner of the FDA, supported a proposal which would have made the categories consistent and would have eliminated the prior sanction exception.

I would like to close by making just two additional points.

First, it is important to recognize that no law is perfect. It will always be possible to find an example of a substance that does not quite fit into a statutory scheme, a substance that is right on the edges of the regulatory statute. If saccharin is such a substance, then it may have been appropriate for Congress to overrule the FDA's saccharin decision, but I do not think that we should allow the single example of saccharin to justify a complete overhaul of the statute that would allow numerous other additives on the market for which an exception of the kind made in the saccharin case simply could not be justified.

Second, I hope that Congress will persist in asking anyone who advocates lowering the safety standards applicable to food additives to identify exactly what the problem is. For example, Senator Quayle, you asked this question earlier, and two examples were given—aflatoxin in peanuts and corn. Aflatoxin is not a food additive. Peanuts and corn containing aflatoxin have never been regulated under the food additives section. The definition of safe does not apply to those substances. The Delaney clause does not apply to those substances. Those foods cannot be used as examples for amending this statute.

I think that advocates of statutory change should be required to identify exactly what past FDA decisions they would overturn, what additives they think ought to be on the market that aren't on the market. If there are very few such examples, then in my view the statute should not be amended. In other words, let's not fix something that isn't broken.

Thank you.

[The prepared statement of Mr. Schultz follows:]

TESTIMONY ON FOOD SAFETY LAWS
before the
Senate Committee on Labor and Human Resources
June 10, 1983
William B. Schultz, Attorney,
Public Citizen Litigation Group

Mr. Chairman and Members of the Committee, thank you for the opportunity to testify at these hearings. My name is William B. Schultz. For the past seven years I have been an attorney with the Public Citizen Litigation Group, which is a public interest law firm founded by Ralph Nader. I have frequently represented Public Citizen and the Public Citizen Health Research Group at the Food and Drug Administration and in federal courts on matters concerning the implementation and adequacy of our food safety laws.

I have written comments on S. 1442, the bill to amend the Food, Drug and Cosmetic Act that Senator Hatch introduced in June 1981. I have also submitted comments on behalf of a number of consumer groups and labor unions concerning proposals which the Reagan Administration is considering that would amend the same law. Those proposals would weaken the food safety laws by changing the definition of what is deemed to be "safe," repealing the Delaney Clause, and by a number of other procedural devices which would make it easier to use food additives that had not been proven to be safe in the food supply. If adopted, the proposals would also make it harder to take additives off the market, even after they have been found to be unsafe. I have submitted both of these documents for the Committee's review, and ask that they be included in the record. In my testimony today, I will try not to repeat the points which are made in those comments.

The purpose of these hearings is to review the adequacy of laws enacted more than 20 years ago. In particular, food additives are regulated by the Food Additives Amendment of 1958; color additives, by the Color Additive Amendments of 1960; and animal drugs, by the Animal Drug Amendments of 1968. Congress recognized when it passed these laws, as it implicitly recognizes when it enacts any statute, that they might some day become outdated. For example, the Delaney Clause, which is incorporated in each of the three statutes, is based on the scientific assumption that an animal carcinogen poses a risk of cancer to humans. The question which we should be answering today is not whether the food safety laws, including the Delaney Clause, will work forever. Instead, the relevant questions are, have those laws worked in the past, and are they working today.

We submit that the facts support an affirmative answer to both of these questions. Only once in the past 25 years has Congress concluded that the result dictated by these statutes was inappropriate. In that instance, it intervened and reversed the FDA's decision to ban the use of saccharin as a food additive. In our view, the only justification for permitting the continued sale of saccharin was that Congress perceived there to be an overwhelmingly public demand for the substance. However, before deciding whether to support proposals to amend the food safety laws, the question which you should ask is whether there are examples of other additives which the FDA has banned or refused to approve, but which you believe should be available to consumers.

If the answer is "no," as we believe it is, then in our view the single example of saccharin should not be used as a justification for adopting wholesale changes in the laws regulating food and food additives.

I would now like to turn briefly to the arguments advanced in support of repealing the Delaney Clause, since this issue seems to be a central focus of every discussion on food safety legislation. The Delaney Clause reflects Congress' view that the possible "benefits" of food additives do not outweigh the risk of cancer, however small. Thus, in the Delaney Clause, Congress required the removal from the market of any substance shown to cause cancer in animals.

There are essentially three arguments which are made in support of such a repeal. The first is that the Delaney Clause does not allow the FDA sufficient scientific discretion. As the argument goes, the Delaney Clause requires the FDA to ban an additive where a single animal test has shown the additive to be a carcinogen, even if the animal study is flawed. This is not correct. In fact, the Delaney Clause retains a large amount of scientific discretion for the FDA to determine whether a substance is an animal carcinogen. For example, even after its own study had found that saccharin causes bladder tumors in laboratory animals, the FDA waited five years until additional studies had reached the same conclusion before it banned saccharin as a food additive. Thus, the Delaney Clause gives the FDA authority to determine the quantity and quality of scientific evidence that must be provided before such a decision is made. However, once the agency has concluded that a substance is an animal carcinogen, Congress, through the Delaney Clause, has removed the agency's discretion to allow it to continue to be sold.

The second argument is that modern science has made the Delaney Clause obsolete because we can now measure minute quantities of substances, such as food packaging materials, which can migrate to foods and are considered food additives subject to the Delaney Clause. The argument is that the amounts, which often involve only a few parts per billion or even a few parts per trillion, are so small that there is no genuine health concern.

While it is true that it is possible to read the statute as requiring that such substances be banned, it is now clear that such an interpretation is legally incorrect. In Monsanto v. Kennedy, 613 F.2d 947 (1979), the United States Court of Appeals for the District of Columbia held that the FDA had inherent authority to exempt small quantities of substances from the food additive amendments, and thus from the Delaney Clause. This exception, sometimes called "the de minimus exception," applies only where the amount which has migrated is very small, for example one part per billion. In addition, under the de minimus exception, the Commissioner must find that, based on the small amount of substance found in the product, allowing the substance to remain on the market "clearly present[s] no public health or safety concerns." Therefore, the second argument for repealing the Delaney Clause depends on an incorrect reading of the statute, which has already been clarified in the Monsanto case.

The third argument for repealing the Delaney Clause is that the scientific assumptions underlying the provision are no longer valid. In essence, the argument is that it is no longer appropriate to assume that an animal carcinogen is likely also to be a human carcinogen. My understanding of the science is that this argument simply is not correct today. We may come to a point in the future where we are able to identify animal carcinogens that are not human carcinogens, and if that happens it will be appropriate to modify the Delaney Clause to take that scientific fact into account. However, insofar as I am aware, no one has yet identified a single example of a food additive which falls into that category, and it is unlikely that we will be able to identify such substances in the future.

When Congress was considering the Delaney Clause in the late 1950's and early 1960's, officials from the Department of Health, Education and Welfare and the Food and Drug Administration testified that the clause was essentially redundant of the general safety clause, which prohibits the sale of additives which are unsafe. They pointed out that, under this provision, even without the Delaney Clause, they would be compelled to ban any food additive shown to be an animal carcinogen. This analysis has turned out to be accurate by and large. In every major instance, including the case of saccharin, where the FDA has banned a significant additive on the ground that it is an animal carcinogen, it would have been required under the general safety clause to ban that additive in any event.

This redundancy does not mean that the Delaney Clause is unimportant. To a certain extent, the Delaney Clause sets the priorities for the FDA by requiring the agency to give elimination of carcinogens serious attention. For Congress to repeal the Delaney Clause would send the wrong signal to the agency, and could result in additional delay in banning dangerous additives, even if such legislative action would not affect the ultimate result.

Although it is not 100% certain that all animal carcinogens are also human carcinogens, this relationship has been shown in numerous instances. Moreover, our current scientific knowledge does not allow us ever to rule out the possibility that an animal carcinogen used as a food additive will cause additional human cancers. In the face of this uncertainty, Congress must decide who should bear the risk: the consumers who could develop cancer and die from ingesting carcinogenic food additives; or the food industry which could be financially harmed as a result of an incorrect decision by the Food and Drug Administration.

Depending on the product, Congress has traditionally struck this balance differently. For example, in the regulation of drugs, Congress has directed the Food and Drug Administration to balance the benefits of drugs against the risks. In certain cases, even carcinogenic substances are allowed in drugs because the therapeutic benefits outweigh the risk of cancer.

Food additives, however, are a different matter. In general, they are either interchangeable or unnecessary. For example, it matters little to the consumer whether the manufacturer uses Red Dye No. 2, another red dye, or no dye at all in manufacturing processed foods. Similarly, most preservatives are interchangeable, and not essential. Therefore, 25 years ago Congress enacted a statute which makes the assumption that any particular food additive has no unique benefits and therefore should not be allowed in food if it is a carcinogen. The theory of the provision is that we ought to eliminate the risk of cancer where we can. Through the Delaney Clause and other provisions of the Food, Drug and Cosmetic Act, we reduce human cancers by lowering our exposure to carcinogenic additives. One can admit that exposure to some carcinogens is unavoidable and still take the position that we ought to have strong laws regulating food additives to minimize our risk of cancer, when possible.

Hearings on the Delaney Clause in 1960 offer an educational example of why it is important to be cautious and of just how wrong the experts can sometimes be. As you will recall, the first Delaney Clause was passed in 1958, but there were no hearings or debate on the provision in that year. Therefore, the hearings on the 1960 Color Additive Amendments contain the first Congressional discussion of the Delaney Clause.

Among the witnesses was Dr. Thomas Carney, a Vice President for Eli Lilly Company.[1] The gist of his testimony was that Congress should not adopt the Delaney Clause because the assumption that animal carcinogens are human carcinogens was simply incorrect. As an example he cited diethylstilbestrol ("DES") which he pointed out had been found to cause cancer in a few species of animals.[2] However, Dr. Carney argued that this substance had been used in human drugs for more than 20 years and was so safe that doctors were prescribing it to thousands of women to prevent miscarriages. He then quoted experts who had concluded that in 1960 DES was safe for humans and that any correlation between DES and human cancer was "most probably mythical."[3]

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[1] Hearings on H.R. 7624 and S. 2197 Before the Comm. on Interstate and Foreign Commerce, 86th Cong. 2d Sess. 265-95 (1960)(hereinafter "Color Additive Hearings").

Twenty years later we know much more. We know that DES causes a rare form of vaginal and cervical cancer in daughters of the pregnant women who took the drug. We also know that approximately 80% of those daughters have an abnormal vaginal condition called "adenosis" as a result of their mother's ingestion of the drug. In addition, a significant percentage of daughters will experience problems during pregnancy as a result of DES, and both DES daughters and DES sons may experience fertility problems. It seems to me that the DES tragedy is an excellent argument for erring on the side of caution, and assuming that if a chemical causes cancer in amimals, it is likely, if not certain, to cause cancer in humans as well.

It may be true that Dr. Carney did not know in 1960, when he and his company vigorously promoted the use of DES as a drug and as an additive for animal feed, that the product would injure so many victims. But the whole point of the Delaney Clause is that in general food additives are not particularly important and, because there is so much we do not know, our laws are designed to require federal agencies to err on the side of safety.

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[2] Color Additive Hearings 266-70.

[3] Color Additive Hearings 268.

We oppose the efforts to weaken the food safety laws. However, we favor strengthening those laws by closing the loopholes which allow food additives and color additives to escape the pre-market approval requirements of the statute and the standards of the Delaney Clause. The most serious loophole is the prior sanction provision in the Food Additives Amendment which allows a large number of additives which have never been tested to remain on the market.[4] Under that provision, an additive which was approved by the Food and Drug Administration or the U.S. Department of Agriculture prior to 1958 may be sold even if it has never been tested for safety. There is simply no basis for treating such additives differently from additives which never received an approval, or additives which came on the market after 1958. In our view, all additives should be required to meet the safety standards of the Act, and therefore we support repeal of the prior sanction provision.

In addition, we believe that Congress should set a firm date in the relatively near future for elimination of the provisional list, which is a list of color additives that the transitional provisions of the 1960 Color Additive Amendments provided could escape the general safety requirements.[5] Those provisions were intended to provide for a two-and-a-half-year testing period, but more than 20 years later there are still several color additives on the provisional list. Incidentally, we believe it is important to note that the legislative proposals drafted by the Food and Drug Administration in 1979, while Donald Kennedy was Commissioner of the FDA, would have provided for the elimination of these special categories of additives which are exempt from the general safety requirements of the statute.

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[4] Section 201(s)(4) of the Food, Drug and Cosmetic Act, 21 U.S.C. § 321(s)(4).

I would like to close with several additional points. First, it is important to recognize that no law is perfect. It will always be possible to find an example of a substance at the edges of regulatory statutes which do not quite fit into the statutory scheme. If saccharin is such a substance, then it may have been appropriate for Congress to overrule the FDA's saccharin decision. But I do not think we should allow this single example to justify a complete overhaul of the statute that would allow numerous other additives on the market for which an exception of the kind made in the saccharin case simply would not be justified.

Second, I hope that Congress will persist in asking anyone who advocates lowering the safety standards applicable to food additives to identify exactly what the problem is. In particular, advocates of statutory change should be required to identify which past FDA decisions the amendments would overturn. If there are very few such decisions, then in my view the statute should not be amended. In other words, "don't fix what ain't broke."

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[5] Pub. L. 68-618, 74 Stat. 399. The transitional provisions are also contained in a note to 21 U.S.C.A. § 376.

Third, if Congress determines, as it did with saccharin, to allow the sale of substances which do not meet the standards of the statute, it should require warning labels on those products so that consumers will be fully informed of this new risk. Such labeling is fully consistent with the freedom of choice argument that is sometimes made by proponents of weaker food safety laws.

* * *

The United States has one of the strongest food safety laws in the world, and probably the world's safest food supply. Those laws have worked extremely well for the past 25 years, and in fact Congress has overruled the Food and Drug Administration only once, in the case of saccharin.

There is a lot at stake in this debate on food safety legislation. Consumers have a lot to lose if the food safety standards are weakened. Industry also has a lot to lose since it could lose the confidence which consumers currently have in the safety of the food supply. For these reasons, I think we should all be very skeptical of the proposals to change the law, and be very cautious about supporting such proposals.

Thank you very much. I would be happy to answer any questions.

(Note: In the interest of economy, certain additional appendix material accompanying Mr. Schultz' statement was retained in the files of the Committee.)

The CHAIRMAN. Thank you, Mr. Schultz.

Dr. Jacobson, we will turn to you now.

STATEMENT OF MICHAEL F. JACOBSON, PH. D., EXECUTIVE DIRECTOR, CENTER FOR SCIENCE IN THE PUBLIC INTEREST, WASHINGTON, D.C.

Dr. JACOBSON. Thank you very much, Senator Hatch and Senator Quayle.

I am the executive director of the Center for Science in the Public Interest, a group supported by 30,000 members. We work on health and environmental issues, and I personally have been following food additive debates for some 13 years now.

America's food supply is undoubtedly one of the safest and most hygienic in the world. Our food safety laws have saved thousands of lives over the years. The public's confidence in the basic safety of our foods, in fact, is the basis on which the multibillion-dollar processed food industry is built. It is in that context that we are extremely troubled by efforts to weaken our food safety laws, particularly with regard to cancer-causing chemicals.

When I first investigated food additives back in 1970, I assumed that the modest amount of animal testing done was adequate to give one a good idea of the safety of the chemical. Several instances since then made me recognize the weaknesses of the animal testing.

Cobalt sulfate was a foam enhancer used in beer in the 1960's. FDA and everyone else knew the chemical was safe. Cobalt is part of vitamin B-12. Unfortunately, cobalt sulfate killed dozens of beer drinkers in the United States, Canada, and Europe. It was subsequently banned.

In the early 1970's a preservative, diethylpyrocarbonate, was considered the epitomy of safety. It broke down to form carbon dioxide and water, two harmless substances. Yet, scientists discovered that it reacted with a substance in beverages to form urethan, a cancer-causing substance. Diethylpyrocarbonate was banned.

Last year we identified numerous studies that showed that hundreds of thousands of people, especially asthmatics, could have sometimes severe reactions to sulfiting agents, preservatives used in many foods and essentially all wine. We identified at least one person, an Arizona man, who was killed by this chemical after eating a salad at a restaurant outside of Phoenix. Sulfiting agents have not been banned.

The only reason that sulfiting agents and cobalt sulfate were discovered to be harmful was that they caused an almost immediate fatal or near fatal reaction. If they had caused cancer or a subtle behavior problem, they never would have been suspected of being harmful and they would have continued to be welcome, assumingly safe additions to the food supply.

If a risk-benefit analysis had been made on either of these chemicals, you ask the question, will they kill anybody? The risk-benefit analyses would have said, no, they are perfectly safe.

Sodium bisulfite, a sulfiting agent, would never cause problems, according to some tests—there was no reason to believe that it would cause these anaphylactic reactions and kill people. There was no reason to believe cobalt sulfate would cause congestive heart failures. The risks would be much less than one in a million. It would be a zero risk according to a risk assessment.

Though companies whose chemicals have proven unsafe complain that current tests are far too sensitive, sulfiting agents, cobalt sulfate, and other additives have highlighted weaknesses of current testing. Animal studies cost hundreds of thousands of dollars and take several years to conduct, but they are still not very reliable. Usually only 50 or 100 animals are given a particular dosage of the test chemical. Each animal represents upward of 2 million people.

While exaggerated dosages partially compensate for the small number of animals, other considerations illustrate weaknesses of the test. Lab animals live for only 2 years compared to 70 for many people. Chemicals are usually tested on only one or two highly inbred strains of animals, whereas humans are genetically extraordinarily diverse. Some people have asthma. Some people are heavy drinkers. Some people have weak livers. These people are at heightened risk in the face of many chemicals.

Lab animals are fed a highly purified diet and are protected totally from alcohol, tobacco, air and water pollutants, drugs, germs, and other food additives, with which particular food additives might react.

Due to such factors, the tests conducted to measure the safety of food additives are inherently insensitive. Any indication whatsoever that a chemical promotes cancer or other health problems should be viewed with the utmost gravity, rather than looking for some reason to excuse the chemical, as we have heard some witnesses testify.

We never had, and never will have, a perfectly safe food supply. Natural contaminants and environmental pollutants have introduced risks for centuries. However, we can—and I believe must—halt the intentional addition of questionable additives to our food supply.

To protect the public adequately, we urge several things:

The prior sanction exemption should be rescinded.

Additives should be tested for their effect on the most vulnerable individuals rather than just on the most healthy.

Additives should be licensed for a given period of time—for example, 10 years—at which point further use would depend upon whether the safety testing met current standards. Currently, virtually no food additive that has been in use more than 5 years meets current standards. Once they are in, it is virtually impossible to get additional testing.

Additives should be tested both alone and in combination with other commonly consumed chemicals to detect possible interreactions that might lead to serious health problems or even death.

Changes in the law to reflect these recommendations would make it easier for the FDA to identify and protect the public from unsafe food additives.

While I have spoken about ways in which the laws should be tightened, some people have urged that the laws should be weakened. Some scientists and policymakers have endorsed the methodology of risk assessments to determine the safety of food additives.

While risk assessments can provide a rough estimate of risk, only a scientist suffering from a bad case of hubris would read too much into the actual numbers.

Basing regulatory decisions on risk assessment is dangerous business, as Assistant Secretary for Health, Edward Brandt, recognized when he stated recently, and I quote accurately:

> Risk assessment is not an inappropriate approach to the problems of regulation. Rather, the real problem is that we simply do not yet have the appropriate scientific base to use risk assessment with full confidence in making many regulatory decisions.

You do not want to force these administrators to always use risk assessment. It doesn't make sense. They never would have found that cobalt sulfate was a deadly chemical from the inadequate kinds of tests that the chemicals are subjected to.

Some have suggested using a one in a million standard for allowing cancer-causing chemicals in our food. Though one in a million is certainly a small fraction, the public should be aware, as you have recognized, Senator Quayle, that the cumulative risk is not necessarily negligible.

Assume that 1 percent of the 13,000 direct and indirect additives cause cancer at the rate of one in a million. Each of the 130 cancer-causing chemicals would cause about three cancer deaths per year, or a total of about 400 per year and 28,000 over the lifetime of the population. Negligible? People will differ in their opinions.

I might point out that the seven people who were killed by tainted Tylenol represented one in a million Chicago area residents.

That concludes our oral statement. I would be pleased to answer any questions you might have subsequently.

[The prepared statement of Dr. Jacobson follows:]

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TESTIMONY

Food Safety Legislation

Committee on Labor and Human Resources
United States Senate

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Michael F. Jacobson, Ph.D.
Executive Director

June 10, 1983

My name is Michael Jacobson. I am executive director of the Center for Science in the Public Interest, an organization that focuses on health and environmental issues. Our non-profit group is supported largely by the donations of 30,000 members.

For the past decade, we have monitored the safety and testing of food additives and have been involved in numerous rule-making proceedings. We have filed several petitions with FDA and USDA regarding the use of food additives. In addition, we publish educational materials about food additives for teachers and the general public. I, personally, have followed food additive issues since 1970 and am the author of Eater's Digest, a book detailing the testing, safety, and use of the most common food additives.

I have criticized the safety and use of a number of food additives in the course of my work. However, by academic training, I am a chemist and microbiologist and am hardly suffering from chemophobia. In fact, I, like many scientists, usually believed almost instinctively that a chemical should be considered safe until proven harmful, especially when I have some reason to believe that a familiar chemical is safe. Several experiences, however, have instilled a great deal of humility concerning the reliability of "common sense" and animal studies.

This first hit home a decade ago in connection with a fairly new food preservative, diethylpyrocarbonate (DEPC). Everyone thought that this was the ideal preservative, because it quickly breaks down into carbon dioxide and water, two harmless substances. Nature plays tricks on us sometimes, though, and this was one time. Just before it breaks down, some of the diethylpyrocarbonate reacts with ammonium that may be in a food to form urethan, a cancer-causing chemical. In 1972, FDA banned this additive that everyone believed was safe. Yet, FDA still does not test additives in combination with other commonly consumed chemicals to detect possible interactions that might lead to health problems.

In the mid-1960s, the brewing industry in the U.S. and abroad started using a new chemical, cobalt sulfate, to stabilize the foamy head on beer. A noble purpose, most assuredly, and everyone assumed the chemical was safe. After all, cobalt is part of vitamin B-12, and sulfate is innocuous. A funny thing happened, though. Waves of congestive heart failure swept through towns--including Omaha and Quebec City--whose shops sold beer in which the additive was used. After some period of surprise and frustration at seeing middle-aged men die unexpectedly, doctors traced the problem to the cobalt sulfate. The chemical is ordinarily safe, but to everyone's surprise turned out to be deadly to people whose hearts have been weakened by alcohol. Additives, however, are still tested on the healthiest, strongest animals available, never on animals whose bodies are weakened by alcohol or other drugs.

More recently, many asthmatics have been reporting asthma attacks after eating dried fruit or salads in restaurants. Some people have had near fatal-reactions. In one tragic case, an Arizona man died after eating in a restaurant. Excellent studies have proven that many people, particularly asthmatics, are extremely sensitive to a group of additives called sulfiting agents. These chemicals are used cosmetically to prevent discoloration in various foods, including chopped lettuce, dried fruit, and "fresh" shrimp. Sulfiting agents have been used for centuries and FDA proposed last July that they be affirmed "Generally Recognized As Safe." Again, sulfiting agents never caused anaphylactic reactions in laboratory animals, because they are tested on the healthiest, strongest animals available, never on animals that have special sensitivies or maladies, such as asthma, allergies, hypertension, atherosclerosis, diabetes, arthritis, malnutrition, or other conditions that affect tens of millions of human consumers of food additives.[1/]

The only reason that sulfiting agents and cobalt sulfate were discovered to be harmful to a segment of the population is that they caused an almost immediate fatal or near-fatal reaction. If they had caused cancer, a one percent reduction in IQ, or a behavioral problem, they never would have been suspected of being harmful, and they would have continued to be welcome additions to the food supply. It is knowledge of chemicals like these that has made me very cautious about considering a chemical to be safe for the entire population. Moreover, knowledge of these unfriendly additives has led me to conclude that we need much better testing and tighter laws to protect the public from potentially harmful additives to our food supply.

Some people have suggested that the safety standard for food additives should be changed from "reasonable certainty of no harm" to "negigible risk." Changing this standard means, simply, that the consumer would be at greater risk than he or she is at now. We wonder if the dozens of deaths caused by the food additives I have just discussed would be happily tolerated by the proponents of the "negligible risk" standard.

Examples like sulfiting agents and cobalt sulfate demonstrate the weaknesses of current testing. Despite the fact that animal studies cost hundreds of thousands of dollars and take at least three years to conduct, they are still not very reliable. Usually, only fifty or a hundred animals are given a dosage of the test chemical. Thus, even a large experiment would include only about 500 animals. These animals represent 230 million

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[1/] CSPI has petitioned FDA to ban or severely restrict the use of sulfiting agents, citizen petition submitted October 28, 1983.

Americans. At a given dosage level, each animal represents upwards of 2 million people. While extremely high dosages partially make up for the small numbers of animals, other considerations illustrate weaknesses of the tests:

* lab animals live only two years, compared to 70 years for humans;

* chemicals are usually tested on only one or two highly-inbred strains of animals, whereas Americans are, genetically, extraordinarily diverse. Certain individuals, however--such as diabetics, alcoholics, hypertensives, allergy-sufferers, and marginally malnourished people--are likely to be much more sensitive to an additive than the test animals;

* lab animals are fed a highly purified diet and are protected from alcohol, tobacco, air and water pollutants, drugs, germs, and other food additives. Interactions between the chemical being tested and other chemicals the animals (or humans) encounter might promote cancer or other health problems. Some tests indicate that BHT, sulfiting agents, and other additives interact with other chemicals to increase the risk of cancer, yet these additives are not tested in combination.

Due to such factors, the tests conducted to measure the safety of food additives are inherently insensitive. Any indication whatsoever that a chemical promotes cancer or other serious health problem should be viewed with the utmost gravity. In reality, though, indications of hazard trigger apologies or more studies rather than action.

With industry pushing strongly from one direction, government agencies usually interpret tests in the most favorable light possible. The FDA maintains that it must have air-tight evidence before it can remove a food additive or prior sanctioned chemical from the food supply. The FDA also accepts the burden of proof for showing that currently used additives, particularly those prior sanctioned, are definitely harmful before taking remedial action. What this means for the public is that our food supply includes a number of additives for which there is some--but not conclusive--evidence of carcinogenicity or other forms of harmfulness.

The contention by some defenders of additives that FDA bans additives "at the drop of a rat" is patently ridiculous. The caffeine added to soda pop, the BHT and possibly BHA added to many snack foods, and the artificial colorings added to candies, breakfast cereals, and soda pop are some of the chemicals that would be banned, if the FDA were enforcing the law strictly.

However, they now remain in billions of pounds of food. One hopeful sign is that some companies are advertising the additive-free nature of their products as a virtue. Even this practice, however, is questionable, since the overall healthfulness of these products is doubtful.

We never had and never will have a perfectly safe food supply. Natural contaminants and environmental pollutants have introduced risks for centuries and will continue to do so for centuries more. However, we can, and I believe must, halt the intentional addition of questionable additives to our food supply. Cancer, of course, has been the major concern, but as the sulfiting agents and cobalt sulfate tragedies indicate, other effects can be just as deadly.

To protect the public adequately, we urge two courses of action: strengthen the law and enforce the law more rigorously. We suggest the following measures:

1. The "prior sanction" exemption for additives in use when the 1958 food additive law was adopted should be rescinded. As caffeine, nitrite, sodium chloride, lead, and other additives have proven, a prior sanction does not assure safety, but does constitute a refuge from regulatory action for long-used substances that may be harmful.

2. Additives should be tested for their effects on the most vulnerable individuals, rather than just on the most healthy; animal models should be used where possible; otherwise, human studies may sometimes be feasible.

3. Additives should be licensed for a given period of time, for example, ten years--at which point further use would depend upon whether the safety testing met current standards. This would insure that problems which have occurred with cyclamate, saccharin, and other GRAS chemicals that were previously assumed to be harmless just because they had been used for decades, would not occur in the future. FDA is finding that very few existing additives have been tested to the same extent that is now required of new additives.

4. Additives should be tested both alone and in combination with other commonly consumed chemicals to detect possible interactions that might lead to health problems.

5. Chemicals need to be tested for effects on behavior. Maximum intelligence, eye-hand coordination, sense of balance, and ability to relate to one's family and neighbors are just as important for one's well-being as a healthy liver and gall bladder. Caffeine, sugar, and possibly other substances in our food are known to affect behavior. Before some tragedy is discovered, we need to institute systematic testing to insure that a widely used additive does not affect the brain and central nervous system and modify the very way we think.

Changes in the law to reflect these recommendations would make it easier for the FDA to identify and protect the public from unsafe food additives.

While I have spoken about ways in which the laws should be tightened, segments of the food industry have indicated that the law should be weakened. I would like to address some points frequently raised.

Improved animal testing methods and increasingly sensitive analytical chemistry methods have proven that a number of chemicals previously thought safe actually promote cancer or are contaminated with tiny amounts of carcinogens. For obvious reasons, food and chemical companies are distressed when one of their products is cited as a possible cause of cancer. Many consumers are also distressed and concerned when the safety of familiar foods is thrown into question. Rather than beheading the messengers of grim news, I believe we should express gratitude to scientists who have developed and used new methods to assay the safety of chemicals. The small number of harmful additives that have been identified should be eliminated as quickly as possible to ensure that consumers are protected from unnecessary risks.

At the same time, I recognize certain difficulties: first, sensitive tests can find vanishingly small amounts of dangerous contaminants in otherwise safe food additives. I believe that the courts and FDA have taken a sensible course, but one that requires continued, close scrutiny. Those bodies have interpreted the law to mean that cancer-causing contaminants or indirect additives would be tolerated if they are present in trivial amounts. If the scientific and mathematical methods used to define "trivial" insure that the cancer-causing additions to food cause no harm, then we can breathe easier over this de facto exception to the Delaney clause. However, we should also recognize that it is still impossible to determine with any degree of certainty the risk posed by any chemical to the very large and heterogeneous American population, as the two "safe" chemicals that I discussed earlier--cobalt and sulfite--proved with such deadly impact.

Some scientists and policy-makers have strongly endorsed the methodology of risk assessments to determine the safety of food additives. While risk assessments can provide a rough, ball-park estimate of risk, only a scientist suffering from a bad case of scientific hubris would read too much into the actual numbers generated by a risk assessment. On the one hand, a conservatively done analysis might exaggerate the actual threat posed by a chemical. On the other hand, risk assessments may dangerously underestimate the actual threat posed by a chemical. Recall that risk assessments would usually be based on just one, or perhaps several, animal studies, the deficiencies of which I pointed out earlier, but deserve reiteration. These studies involve small numbers of genetically homogeneous, short-lived animals maintained in the best of health and protected from noxious chemicals and harmful germs. Such artificial test conditions provide a great deal of information about the effect of a chemical on the animal used, but provide only a mirage of safety as far as people are concerned. We urge that risk assessments be taken with a large grain of salt.

Basing regulatory decisions on risk assessments is a dangerous business, as Assistant Secretary for Health Edward N. Brandt, Jr., recognized when he stated recently:

> Risk assessment is not an inappropriate approach to the problems of regulation. Rather, the real problem is that we simply do not yet have the appropriate scientific base to use risk assessment with full confidence in making many regulatory decisions.2/

Using a "negligible risk" standard for regulating food additives, however, would require precisely what Assistant Secretary Brandt warns we know too little about to use reliably.

It is positively frightening to see how some well-credentialed people would use risk assessments. Peter Hutt, a former General Counsel of FDA and now an attorney representing food processors, has quoted, apparently with approval, Professor Wilson's writings on regulating on the basis of risk assessment: "Wilson has suggested that, based upon linear extrapolation from animal testing, [chemicals indicating] a risk of higher than 1 in 100 should be banned, a risk lower than 1 in 100,000 should be regarded as trivial, and a risk between those two levels should

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2/ Brandt, Dr. Edward N., Testimony before the Subcommittee on Department Operations, Research and Foreign Agriculture; House Committee on Agriculture, Feb. 22, 1983 be subject of public education, warnings, and efforts at reduction."[3]

Let us look at what Wilson's "ban risks higher than 1 in 100" policy would mean for the public. Approximately 4 million babies are born annually in this country. Approximately 3,000 substances are added to our food supply intentionally, and another 10,000 indirectly. Assume that just one percent of these 13,000 chemicals posed a cancer death risk of "1 in 100." Applying that risk of death to the 4 million babies, each one would have 1.3 fatal tumors. Every single baby would die of a food additive induced cancer. If only one one-hundredth of one percent of the 13,000 chemicals caused a 1 in 100 risk of cancer death, 52,000 babies would still be killed by the additives. Because these deaths would occur years after first ingestion of the additives, they would never be linked to the additives. The deaths would largely be invisible to those concerned with food safety policy. It is likely that the apparent absence of food-related cancer deaths would be cited several years hence as an excuse to weaken the law even further. It is proposals such as Wilson/Hutt's that lead me to conclude that the slope of risk assessments is a slippery one indeed and that our basic food safety laws should not be weakened any further than the courts and FDA have already defined.

Others have suggested using a "1 in a million" standard for allowing cancer-causing chemicals in our food. Though 1 in a million is certainly a small fraction, the public should be aware that the cumulative risk is not necessarily "negligible." Assume again that one percent of the 13,000 direct and indirect additives caused cancer deaths at a rate of one in a million. Each of the 130 carcinogenic chemicals would cause about 3 cancer deaths per year, or a total of about 400 per year and 28,000 over the lifetime of the population (assuming everyone lived to 70 years of age). Negligible? That is certainly a matter of debate, particularly when you yourself or a loved one was one of those to be sacrificed on the altar of "negligible risk."

A second difficulty that arose (and then disappeared quickly) only once might be called the risk/risk dilemma. In theory, at least, an additive that protects the safety of the food supply may introduce its own dangers. This was said by some to be the case with sodium nitrite, a preservative used in cured meats. The dilemma evaporates if other, safe, additives or methods are available and could practically replace the questionable chemical. However, it is conceivable that some protective additive might be unique. In such cases, it would seem reasonable to try to quantify the two risks as accurately as possible (not a simple undertaking!) and then decide whether it would be better to permit or prohibit the use of the chemical. However, I do not believe the current law should be changed to allow for this situation, because the existence of such an additive is more hypothetical than real. If such a problem ever arises, Congress could deal with it as a special case, as it has done with saccharin. The fact that special cases have arisen only once or twice in twenty-five years means that the current law is working quite well. If only other laws had such a good record!

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[3] Hutt, Peter Baron, "Unresolved Issues in the Conflict Between Individual Freedom and Government Control of Food Safety", Paper presented to Conference on Public Control of Environmental Health Hazards, New York Academy of Sciences, New York, NY, June 29, 1978, pp. 33-34.

Third, we would like to comment on the argument made by some that since natural foodstuffs contain cancer-causing chemicals, we should relax our regulation of intentional additives. First, we would emphasize the illogic of this argument. Just because something in a traditional food poses some risk hardly means we should reduce our concern about food additives. Our goal should be to maximize the safety of our foodstuffs, giving due respect to long-time cultural patterns and minimizing disruption of the food supply. If problems exist in traditional foods, alternatives should be sought, but we should continue to exercise vigilance over intentional additives, whose risks could be avoided quite simply just by not adding them to otherwise safe food.

We would also chide food industry spokespersons for exaggerating the risks associated with natural foods. In June, 1978, Peter Hutt published a paper in the Food Drug Cosmetic Law Journal in which he described numerous, allegedly cancer-causing chemicals in widely used foods and condiments. His list included calcium, caffeine, lactose, maltose, and other substances.

Ignoring the bizarre fact that the food industry itself was shedding doubt on the safety of the food supply, we discovered that Hutt's list was highly misleading. We discovered that his paper included non-existent and incorrect journal references, claims rejected by the authors of the papers, and bits of evidence that would be deemed by the FDA to be totally inadequate to demonstrate carcinogenicity. (See Appendix A).

That concludes our prepared statement. We appreciate your listening to our concerns about the safety of the food supply and our suggestions for improving national policies. I would be pleased to answer any questions you may have.

4/ Hutt, Peter Barton, Food Drug Cosmetics Law Journal, October 1978, pp. 558-589.

(Note: In the interest of economy, the appendix accompanying Dr. Jacobson's statement was retained in the files of the committee.)

The **CHAIRMAN**. Thank you, Dr. Jacobson.

Mr. Mayer, we will conclude with you.

STATEMENT OF ARNOLD MAYER, INTERNATIONAL VICE PRESIDENT, UNITED FOOD AND COMMERCIAL WORKERS INTERNATIONAL UNION, WASHINGTON, D.C.

Mr. **MAYER**. Mr. Chairman and Senator Quayle, I am Arnold Mayer. I am a vice president and the director of government affairs of the United Food and Commercial Workers Union.

The UFCW is a labor union with 1.3 million members, most of whom work in the food industry.

I would like to avail myself of the chairman's suggestion and put my statement in the record. Instead, I would like to make a few commonsense comments on what has transpired this morning and on the hearings in general. I know I do that at the expense of seeming either anti-intellectual or emotional, but the fact is that we are not dealing with intellectual games here. We are talking about a subject that involves, if errors are committed, human suffering, human illness, and human death. We are talking about substances that can cause cancer. So there is a rather emotional aspect to this.

I do not know whether or how near zero protection can be achieved, but I do know that the majority of the American people expect to be protected to the maximum degree. They think their Government is doing that, their laws are doing that.

I think that expectation is particularly relevant when one realizes that cancer seems to be an illness that builds up over a 20-year or 30-year period. Therefore, any little addition has a consequence and a rather serious consequence.

Now we have heard about these great scientific developments and the marvelous tests that have been developed over the years, and I wonder whether those tests can be used to provide as great a protection as possible, rather than as an excuse to dilute the food safety laws.

In terms of the negligible risks, I think it is a political question whether Congress wants to say, or whether any part of the Government should say, that the risk of 1 in a million or 1 in 10 million is OK and, therefore, that 250 people shall die from cancer or 25 people shall die. That is a political decision. Should that political decision be made? That, I think, is one of the decisions that this committee and the Congress has to consider.

One of the witnesses this morning says that we are dealing with probability levels rather than real life. I assume the probability levels have some relationship to real life, because if they don't, then what are we talking about?

If that negligible risk hits someone in my family, I assure you that I would consider it a rather devastating, soul-wracking experience—and not a negligible risk. I think other families would feel the same way.

We had a rather amusing and delightful interlude this morning about foods that would have to be banned. I listened and realized that only one of two conclusions is possible. Either there is flexibility in the Delaney clause, because the foods have not been banned by the Government or the administrators who sat here, in front of you, are not doing their jobs.

We also heard of the tough time that the Food and Drug Administration is having enforcing this legislation. I think it is important to note that the objective of these three food safety laws is not to make work easier for the Food and Drug Administration or the Agriculture Department or easier for its administrators, but rather it is to protect the public. I think that is the objective.

If there are frustrations, it is sad that they exist, but the basic question is: Is the health of the public being protected?

There have been cases—nitrite was mentioned and saccharin—where the regulators had to throw up their hands and the issue went or almost went to Congress. At the expense of adding work for Congress, I think that is good.

I think that the public debate that took place on saccharin served a public end. I think the fact that the decisions involved became clear to the public is desirable. The fact that this decision over life and death, or life and illness, was made by elected officials is good.

If the studies on nitrite had not been flawed, if nitrite had been proven to be cancer causing in and of itself, my union—I will admit to you—would have been here with other groups to ask for a phaseout. We would have done that because we would have seen the quick and immediate end of nitrites as bringing chaos to the industry and as causing unemployment. We would have pointed that out.

Why should it have been made easy for us to do that? Why shouldn't we have had to do that in the public debate? Why shouldn't there have been a public balancing of whether that factor outweighed whatever the health problems were?

I think that would have become a political decision, and that is something which I think only Congress—not the bureaucracy—can address itself to on a case-by-case basis.

We are not dealing here with something that people can make a quick decision on their own on. If people want to smoke and open themselves up to the possibility of cancer, that is their business. The knowledge is there. The information is there.

However, with additives, you are dealing with substances that people do not know that they are eating and have no idea and cannot really find out. Here, the public really has to be protected. This is not a case of big brother. This is a case of providing the protection which people need and cannot get for themselves.

Thank you very much.

[The prepared statement of Mr. Mayer follows:]

UFCW

Arnold Mayer
International Vice President
Director of Government Affairs

STATEMENT BY ARNOLD MAYER
INTERNATIONAL VICE PRESIDENT AND DIRECTOR OF GOVERNMENT AFFAIRS
UNITED FOOD AND COMMERCIAL WORKERS INTERNATIONAL UNION (AFL-CIO)
PRESENTED TO THE COMMITTEE ON LABOR AND HUMAN RESOURCES
OF THE UNITED STATES SENATE
JUNE 10, 1983

My name is Arnold Mayer. I am an International Vice President and the Director of Government Affairs of the United Food and Commercial Workers International Union (AFL-CIO).

The UFCW is a labor union with 1.3 million members organized in some 700 local unions throughout the United States and Canada. The UFCW and its local unions have collective bargaining agreements with tens of thousands of employers throughout the food processing, retail sales, fur, leather, health, commercial, shoe and other industries.

Mr. Chairman and Members of the Committee, we appreciate the opportunity to appear at your important hearings. Since a large majority of our members work in the food industry, the UFCW has long been concerned about consumer protection involving food products.

Our union believes that the nation's food safety laws provide for strong protection of the public health and that neither the public, the food industry, nor this Congress would be served by diluting these protections. Instead we urge that this Committee and the Congress provide the federal food safety agencies --the FDA and USDA-- with the additional authority they need to enforce these standards and to ensure that the underlying goals of the Food, Drug and Cosmetic Act, as well as the Federal Meat and Poultry Inspection Acts-- are achieved and that the public health is protected from chemical and other hazards in the food supply.

NO NEED FOR WEAKENING

The major impetus for changing the food safety laws seems to come from some trade associations which are concerned about their members' ability to freely use certain materials. The soft drink makers are concerned about saccharin, parts of the meat industry about nitrite and the plastics manufacturers about food packaging. Yet, in each of these cases, there is no practical problem today which would warrant any modification in the food safety laws, much less the sweeping overhaul which has been suggested.

The use of saccharin continues because the Congress intervened in the FDA decision process in response to the perception of wide public demand for the artificial sweetners. Nitrite is still used because scientific judgment did not support regulatory action to remove the additive from the market. And plastic packaging is in wide use because the U. S. Court of Appeals determined that the FDA has discretion when it determines that the chemicals which enter food as indirect additives clearly pose no health hazard.

In addition, we have not heard of any additive which would greatly benefit the public and would be put into the food supply if the FDA would or could permit its use. We, therefore, fail to see the problem or the need to dilute the safety standards in the three food safety laws.

Obviously, regulatory legislation is not to everyone's liking --especially those being regulated. But it was not enacted to please everyone or to satisfy the industries being regulated. It was established in long and difficult legislative battles to protect the health, safety and pocketbooks of consumers.

It should do that to the maximum degree. If any error is to be made concerning food safety legislation, certainly it should be made on the side of caution and public safety --particularly when we are dealing with substances which may cause the dreaded illness of cancer.

PUBLIC CONFIDENCE AND SAFETY

Public concern over the federal government's willingness and ability to protect the nation from health or environmental hazards is already at an all time high. To make changes in the laws which could lead to serious dilution of public protection --or even suspicion of serious dilution-- would only shake the public confidence. It could only hurt industries and workers and contribute to the serious economic problems and joblessness which already exist.

The subject you are dealing with is not simply one of scientific pros and cons to be decided by wise and dispassionate experts. As you have already found, experts disagree and there is no absolute, unarguable body of knowledge. Choices have to be made based on differing premises and objectives. And those premises and objectives are very vital considerations.

Even more important, the cost of error in this area is very high. It is greater than some added cost of production or not being able to add color to some product better and more efficiently or not being able to add another taste to the market for public consideration. The cost of error is human suffering, human illness and human death.

SOME STRENGTHENING PROPOSALS

If the food safety laws are to be changed, the UFCW urges that the Congress consider the many changes proposed in recent years to enhance the ability of food safety agencies to control hazards. The General Accounting Office in a 1979 report, for example, proposed the following:

* Amend the Federal Meat Inspection Act and the Poultry Products Inspection Act to provide USDA quarantine authority to prevent the marketing of additional animals by a violative grower until corrective action has been taken.

* Amend the Federal Meat Inspection Act and the Poultry Products Inspection Act to authorize USDA to require growers to place identification tags on animals before they are sent to an auction house or slaughterhouse.

* Amend the FD&C Act to make the misuse of an animal drug a violation of the Act.

* Amend the FD&C Act to provide FDA authority to levy civil penalties for violations of the Act's provisions.

* Amend FIFRA to provide EPA authority to inspect a grower's premises for the purpose of identifying possible misuse of pesticides likely to result in residues in food.

These are only a few proposals by one government agency. There are many others proposed by many private and public study groups to make the food we consume safer.

GREATEST EXTENT POSSIBLE

Our nation is blessed with an abundant, widely-varied and relatively inexpensive food supply. Any increased public risk from diluting our food safety standards would certainly outweigh any benefits in terms of additional colors or flavors in food or even fractional savings on individual food product prices.

When the Congress set down the strict safety standards for food and food additives 25 years ago, it reflected broad public concern about cancer and a policy decision to control cancer risks to as great an extent as possible. Those concerns and policy needs continue to exist today. The consumer does not need weaker food safety standards but stronger tools with which the existing standards can be enforced.

The **Chairman**. Thank you, Mr. Mayer.

Dr. Jacobson, we have heard from many distinguished scientists in the last 2 days, including two former FDA Commissioners and eight scientists. Not one supports the body-count interpretation of one in a million risk. Explain to the committee why your position is different from theirs.

Dr. **Jacobson**. From the testimony I heard this morning, I was puzzled, where people said a one-in-a-million risk is not really a one in a million risk. It is a calculation based on one or a very small number of animal studies. It is a risk, and you could say less than one in a million, but one calculates a certain risk. One knows the population of this country, and one could do a very simple division.

It is a ball park kind of estimate. The animals are not people. Humans may be more sensitive or much less sensitive than the particular highly inbred strain of animal used, but it gives you some ball park estimate. However, it is not a very accurate one.

I think Secretary Brandt and Commissioner Hayes said that sometimes risk assessments are useful; sometimes they are not appropriate, and I agree with that. I would hate to write risk assessment into the law. The numbers that one gets have a definiteness that makes them seem accurate. If it says one in 3 million, it sounds pretty accurate. It sounds scientific, but it is just a lot of hand waving.

The **Chairman**. I see. Dr. Jacobson, in the Washington Star several years ago you provided your own approach to risk assessment. Let me read it. I quote:

> Here's my rough—and I emphasize rough—guideline on ranking the risks. One, serious risk; that is, one in 5,000 chance or greater of harming you. Make changes in your own buying or living habits. Personal behavioral changes should be supported by educational campaigns, product recalls, prohibitions when appropriate, and other health and safety promoting regulations.
>
> No. 2, smaller risks—that is, between one in 5,000 and one in 5 million chance of harming you—support regulatory or legislative actions to reduce or eliminate the risk. Personal changes are optional.
>
> No. 3, trivial risks not only to you, but to the population as a whole. That is less than one in 5 million chance of harming anyone. Don't worry about it.

While your numbers are different, you really do not sound all that different from the individuals you claim to be in disagreement with. Do you care to comment on that?

Dr. **Jacobson**. The danger is to incorporate aris-assessment requirement into law. I think in terms both of personal action and of what a society should do, I stand by those kinds of rough estimates.

Getting good numbers, though, is extremely difficult, when you have to use animal studies, when you cannot test a chemical on individuals with different sensitivities.

I would like to be able to use risk assessment. It would be very nice to test a chemical on different types of animals. In some cases human studies might be available, and one might be able to determine with accuracy that a risk is less than one in a million, one in 5 million, whatever the number. It would be nice to regulate on that basis. Unfortunately, we are not at that stage yet because the tests are really rather rudimentary.

It was disappointing to me to see some of the testimony that you have heard from very well-credentialed scientists did not acknowledge the weaknesses in the tests, the fact that the animals are so protected, that animals do not take drugs where most Americans take over-the-counter or prescription drugs.

Risk assessment is not, and probably never will be, well enough developed to come up with that definite dividing point between 1 in 1 million and 1 in 1½ million.

The **Chairman**. As I viewed it during the past 2 days of these hearings, almost every witness would support statutory recognition that in certain food safety decisions the health benefits of the substance are relevant. Do you agree with that?

Dr. **Jacobson**. In terms of food additives, if there is some additive that poses a risk but also protects people from a risk, and that additive is unique, it is not replaceable by a safer additive, I think it makes sense to balance the risk of leaving it in against the risk of taking it out.

It is not a generic issue, though, in that the only example that I ever heard anybody give was nitrite where the benefits are arguable. It is not clear that they really exist. It is not clear that nitrite is not replaceable by other chemicals or other processes.

Second, I think it is worth realizing that measuring the risk of nitrite as a cause of cancer or nitrite as a preventer of botulism are both very difficult to measure and to compare to one another. Again, it becomes a hand waving—who can hire the most scientists to support a particular point of view.

However, in principle, if there were a chemical that is unique and really does provide benefits, I think those benefits should be weighed against its risks. There just aren't any examples.

The **Chairman**. Let me ask the other members of the panel: How do you feel about this issue of benefits versus risk?

Mrs. Foreman?

Mrs. **Foreman**. Yes, sir, Senator.

I think that this balancing can be OK if there is an established health benefit from a product weighing against its health risk, if it has been on the market for a long time, if there are no practicable substitutes available for it. I spell this out in detail in my prepared testimony.

I was certainly willing to ask the Congress to make that balancing with regard to nitrite, not because I think that nitrite cannot be replaced, but I was pretty certain, as the person in charge of meat inspection, that it could not be replaced absolutely immediately without creating some risk.

Nitrite has not been found to be a carcinogen. I do not know any other substances right now that meet that standard. In the absence of such substances, one has to raise some question: Should Congress rewrite the law in a wholesale fashion to accommodate a little man upon the stairs who so far isn't there?

The **Chairman**. Ms. Haas?

Ms. **Haas**. I would like to add to that. The record has shown—and the most recent case is saccharin in the National Academy of Sciences report—that it was, indeed, difficult to prove that there were any health benefits.

Because you are dealing with a different numerator and denominator, the risk of cancer versus weight reduction, or whatever the benefits might be of saccharin, it becomes almost a virtual impossibility and open to political pressues.

I do not think it is appropriate at this time, given our state of knowledge, and I look back to the time of 1958 and 1960 when I think that Congress, indeed, gave the kind of benefit-risk analysis that is necessary and concluded in what I think is their wisdom that there was no benefit that was more than the risk of cancer from the ingestion of only food additives and color additives and later from animal drugs.

The CHAIRMAN. Mr. Schultz?

Mr. SCHULTZ. If I could leave you, Senator Hatch, and you, Senator Quayle, with one thought, it is this: It is a question. The question is: What are the examples where the definition of safe isn't working? What are the examples of food additives that are animal carcinogens that are not human carcinogens?

I would ask the same question here: What are the examples of food additives that have benefits that outweigh their risks?

We haven't seen any except the possible example of nitrite, and I certainly do not think that that is a justification for a wholesale amendment to the statute.

The CHAIRMAN. It seems to me you would have to include saccharin also, and, the health benefits to overweight people, diabetic people, people with heart conditions, and so forth.

Mr. SCHULTZ. I am glad you mentioned the example of saccharin, because the FDA and the NAS both looked at this question when they were considering the ban, and they both said that there are no studies that show that saccharin is beneficial. I do not think that saccharin could be allowed on the market under the standard of any of the legislation that has been proposed.

The CHAIRMAN. But you would still propose that saccharin be banned?

Mr. SCHULTZ. I view the saccharin issue as a decision for Congress, and I think it——

The CHAIRMAN. Well, how do you feel? [Laughter.]

Mr. SCHULTZ. Personally, how do I feel?

The CHAIRMAN. Would you ban it or not?

Mr. SCHULTZ. Personally——

The CHAIRMAN. If you were the head of the FDA and you had life-and-death control that issue, would you ban saccharin?

Mr. SCHULTZ. Oh, the head of the FDA had no choice but to ban saccharin under the statute.

The CHAIRMAN. But you would, also?

Mr. SCHULTZ. Oh, of course.

The CHAIRMAN. Under this statute?

Mr. SCHULTZ. Under this statute——

The CHAIRMAN. Because there is no choice.

Mr. SCHULTZ. And the head of the FDA would have had to have banned saccharin under the bill that you introduced a year and a half ago, under the bill that Congressman Gore introduced, and under the administration's proposal. None of these proposals can deal with the problem of saccharin because the only justification for leaving saccharin on the market is a popular demand, the same justification as used for cigarettes. We certainly would not want cigarettes to be used as a food additive, but yet we allow it on the market for other reasons.

The CHAIRMAN. Well, maybe we'd better write cigarettes into the FDA rule. Some people are advocating us to do that. I just do not agree that I should tell people what they can and cannot eat or what they should and should not smoke even though I personally do not smoke. I understand what you are saying.

Let me ask you, Mr. Mayer—excuse me. You have another comment?

Mr. SCHULTZ. I appreciate that point of view that we should not tell people not to smoke or not to do something that they want to do. However, in the area of food additives, I do not think saccharin is representative. Most people cannot pronounce, let alone name, the food additives that they use. That is why we take a different approach here.

The CHAIRMAN. Senator Quayle has to leave, so let me turn to Senator Quayle.

Senator QUAYLE. Thank you very much. I will take less than 10 minutes, Mr. Chairman I thank you for your politeness.

The CHAIRMAN. There is one problem. I did not let Mr. Mayer answer. Let me just do that.

Do you basically agree with the rest of the panelists, Mr. Mayer?

Mr. MAYER. To conserve time, I basically agree. [Laughter.]

Senator QUAYLE. I do not want to get into a debate on whether the Delaney clause is a position of no risk. I think there is a reasonable difference of opinion on whether it is or it is not no risk.

My question is, should we have a policy of no risk? Should that be our policy—no risk—or not?.

Ms. HAAS. I think it is misleading to ask a question like that so generally, because the basic Food, Drug, and Cosmetic Act is not a policy of no risk. There are different degrees of regulation, and there is only one instance where there is the strongest case, which is only in the case of food additives and color additives. That poses only risk to consumers of cancer.

If you go back, given our current state of scientific knowledge, I have not heard in any of these days of hearings anything very much different than back in 1958 or 1960 where the Secretary of HEW said, "No one knows how to set a safe tolerance for substances in human foods when those substances are known to cause cancer."

I would agree that under those circumstances it is appropriate to have the strictest form of regulation, if you want to call it no risk.

Senator QUAYLE. I do not want to get back into the interpretation of the statute because that is an open discussion. Reasonable people disagree on whether it is no risk.

What I am asking and what I want to get is this: Should we have a policy of no risk? If not, then, as Mrs. Foreman said, how many cases of cancer are we going to consider negligible and insignificant? I think that from a policy determination at least I would like to get your response to that basic policy question. I do not want to get into the statute. I just want to get a response and a feeling whether we should have a policy of no risk. Should that be our policy?

Mr. **Schultz**. I will be glad to give you a direct answer. For food additives that are carcinogens, yes.

Senator **Quayle**. You would say there should be a policy of no risk, but you would——

Mr. **Schultz**. For food additives that are carcinogens, there should be a no risk policy.

Senator **Quayle**. OK. Do you support that?

Mrs. **Foreman**. Let me point out that is the only place in the law now where that applies.

Senator **Quayle**. I understand that.

Mrs. **Foreman**. Yes. I at this point think that there is no justification for changing that on a general basis.

Senator **Quayle**. In other words, you would support a no risk policy for additives?

Mrs. **Foreman**. For cancer-causing additives.

Senator **Quayle**. For cancer-causing additives.

Mr. **Mayer**. Or as little risk as possible. [Laughter.]

Senator **Quayle**. Here we go. What was that? As little risk as possible?

Mr. **Mayer**. Yes. Start as a philosophical——

Senator **Quayle**. That is why I am asking the question? I want to see if there is unanimity on this issue.

Mr. **Mayer**. Philosophically, I think we ought to approach this with no risk, knowing that you can probably never achieve a no risk situation. As a result, in real life, we are left with the greatest protection possible.

The **Chairman**. Could I just interrupt for one second? It is nice to say "food additives," but if you cut up potatoes and put them in a stew, that is a food additive under the law.

Senator **Quayle**. Let's not get off on that subject. [Laughter.]

Ms. **Haas**. I would like to go back to your question. I would like to ask, are you saying—are you willing to accept in the food supply cancer-causing food additives, the risk of cancer-causing food additives? I would say, to answer that, no. Therefore, you might flip it around and say, therefore, that is a no risk policy.

I think you go back to the flexibility that Bill talked about to begin with, that it must be appropriate test before you not allow those cancer-causing additives. It has been a long time in the test for saccharin, and a lot of the other additives that were given today never were banned because the tests never were concluded.

Senator **Quayle**. There is a little window of disagreement on whether we ought to have a policy of no risk or perhaps a policy——

Mr. **Mayer**. No, there is no window of disagreement, Senator. I said that I think philosophically you should approach it at no risk. I think the other side would immediately come back and say that no risk is impossible. However, I think philosophically, if you are asking the question, yes.

Senator **Quayle**. I am struck by—you keep pointing to cancer-causing additives for which we should have the no risk policy, but I suppose you are saying that the no risk policy would not apply to other cancer-causing foods, whether it be the original substance or——

Mrs. **Foreman**. That is correct. That is the way the law reads now. That has been misinterpreted.

Senator **Quayle**. Wait a second. Let me finish. Hang on. I will give you plenty of time to rebut within my 10 minutes.

You are saying that for cancer-causing additives, there is a no risk policy—I know what the law is now. I am not talking about what the law is now. I do not want to get into a discussion of what the law is now. I just want to get your basic, overall policy so I can get a good feeling of where you are coming from and what we are going to have to negotiate on the legislation. To be quite honest with you, that is what I am trying to draw out here.

We have the cancer-causing additives, no risk, but if it has an original substance or pesticides or packaging, then we are saying that the no risk policy would not apply; correct?

Mr. **Schultz**. Not packaging. Not packaging, no.

Senator **Quayle**. In other words, if you got cancer by packaging, that is OK?

Mr. **Schultz**. No, not packaging, I said.

Senator **Quayle**. Oh, you were saying no to——

Mr. **Schultz**. Absolutely apply it to packaging.

Senator **Quayle**. OK. Apply it to additives and packaging. We have two categories now. Do the rest of you——

Mrs. **Foreman**. I think that——

Mr. **Schultz**. You have to understand the Monsanto case——

Senator **Quayle**. I understand the Monsanto case. I understand the de minimis ruling in Monsanto.

What I am trying to get out of you and this panel is a feeling for what we ought to be interpreting in this no risk policy. Now we have a discrepancy in the law, which you all know about very well because there are certain different standards for Delaney, for "safe," and for the substances, origination, additives, pesticides, packaging. Those are all treated differently.

I would think that we might be interested in having an overall policy for all those. If we are going to protect the consumer and we are going to be interested in food safety, it would seem to me that we might want to have a uniform standard, whether it is at the original cause or whether it is additives.

I do not understand why we have to have this distinction.

Ms. **Haas**. I think the law is quite pragmatic and reflects what we can control. For the cases of naturally-occurring substances where we set tolerances, it is because we cannot control all of those substances—also, environmental contaminants.

There is a very different situation for food additives, color additives, and indirect additives like packaging materials. Those are controllable.

Also, the consumer cannot identify the risks that are involved. You can see saccharin. If you are going to be buying spinach and somebody says that spinach contains nitrites and therefore is cancer-causing, you know you can stay away from spinach.

I think that the law is basically very reasonable. I would not personally, nor would Public Voice, advocate a no risk policy for all foods or we would not eat. However, in certain specific instances it is necessary.

Mr. SCHULTZ. It is not just that, Senator Quayle. I think—and I cannot believe anybody in this room would disagree with this—— [Laughter.]

The CHAIRMAN. Let's have order. I want all witnesses treated with respect.

Mr. SCHULTZ. We ought to go as far as we can go in eliminating cancer-causing substances from our environment. Now there are some places where it is easy; there are some places where it is hard.

One of the places where it is easy is food additives, so we ought to have a very high standard there. In places where it is hard, we are going to have to live with the lower standard. That is the philosophy that underlies this statute.

It may seem that these categories are inconsistent, but——

Senator QUAYLE. They are. We have an inconsistent standard. It depends on which particular category a substance falls into. Yet, I think as an overall policy, particularly one which gives the consumer confidence in the administration on an equitable basis for FDA or USDA, or whatever, that we might think about some uniformity within the law.

Dr. JACOBSON. If you wanted uniformity, then you wouldn't just look at food additives or foods. You would say, what about anything that causes health problems, and you would come to the conclusion either that anything that causes less than 100,000 deaths a year shouldn't be banned or you would start talking about banning cars and cigarettes and a whole lot of other things—elevators. It does not make sense to be totally consistent across the board.

Senator QUAYLE. I do not want to be impolite, but I have a time problem. I also have an obligation to my distinguished chairman.

Two quick things: The phaseout that Mr. Mayer talked about, is there any other support for a phaseout proposition, as he describes it—that they would be here testifying for a phaseout of the nitrite——

Mrs. FOREMAN. Yes, sir, and it is spelled out in some detail in the testimony.

Senator QUAYLE. Ms. Haas?

Ms. HAAS. All I would caution is that it be very limited, if it were used, that it be very limited and nonextendable.

Senator QUAYLE. Mr. Schultz?

Mr. SCHULTZ. I do not support it.

Senator QUAYLE. Dr. Jacobson? Yes or no?

Dr. JACOBSON. It is not a yes-or-no question.

Senator QUAYLE. I have one final thing.

Mr. MAYER. Can I——

Senator QUAYLE. Did I misquote you?

Mr. MAYER.Say something there? I suggested that any phaseout be dealt with on a case-by-case basis.

Senator QUAYLE. I know it is just a concept of phaseout. I just wanted to get it——

Mr. MAYER. But——

Senator QUAYLE. Let me just tell you in 30 seconds where I think that Don Kennedy put his finger on the problem in his testimony. It was on page 2 or 3. He said that we must revisit and there must be some legislation because of the maze of regulations that have gone into an act that is 25 years old and hasn't been revisited.

He also went on to say, as I pointed out earlier, that the congressional statute or the statutes passed by Congress should be rather vague. We should try to set some policies, but he thought to clear out that underbrush that had been accumulating over the years, that there were some problems with the actual enforcement and interpretation, and I really concur with that. That is the reason I think that we ought to proceed along.

I think that these hearings have been tremendous, Mr. Chairman. I apologize to our last group. I would like to stay around and hear them. I have talked to them before, and we will be discussing it in the future.

I thank you for your patience and your indulgence. I thank this committee.

The **Chairman**. Thank you, Senator Quayle, for your lively questioning. [Laughter.]

I would like to conclude with this question: The words I keep hearing you all say are basically don't make broad, sweeping changes in the law. I have not heard a single witness suggest that it is necessary or desirable to make broad, sweeping changes in the law.

The limited number of changes that I have heard advocated all sound, I think perhaps with some modification, very reasonable.

Now are your concerns really with these changes that have been suggested or are you afraid that changing the laws—may open up a process that really cannot be kept focused? Is that what you are concerned about? Are you really concerned with any change whatsoever in the law?

Mr. **Schultz**. Senator Hatch, it is both. We are, of course, concerned that it could get out of hand, but we are also concerned with the particular changes that are being discussed. In particular, I think we are most concerned about the change in the definition of "safe." You may be able to do that with a few words, but that is a major change in the statute. The same is true of the Delaney clause, phaseout, and benefits. Those are fundamental changes in the statutes.

The **Chairman**. You are in danger, Mr. Schultz, of being called a conservative because you seem very enamored with the past and afraid to change in the future. [Laughter.]

The **Chairman**. I know that is horrifying to you.

Mr. **Schultz**. No, it is not. As a matter of fact, I gave a speech a year ago in which I characterized myself as a conservative. This was a bill that was passed by a Republican administration. It is a law that has worked very well.

I think we all should be cautious to change this law, and we ought to demand examples of problems.

The **Chairman**. I agree with that.

Mrs. **Foreman**. Senator, let me raise one concern in that regard. If you write "insignificant" or "negligible" into the law and fail to define it, you can have a Commissioner of the Food and Drug Administration who defines that as one in 10 million. I might if I were Commissioner. Senator Grassley would not like that at all.

The **Chairman**. No.

Mrs. **Foreman**. You might have one who would come along after me and define it as 1 in 10. I would not like that. I do not think you would.

The **Chairman**. No.

Mrs. **Foreman**. Now how far are you going to go to restrict this bureacratic regulatory power that Senators tend to not be enamored of most of the time?

The **Chairman**. But which we often tend to create.

Mrs. **Foreman**. Yes.

I am urging you in this case not to let the courts do the interpretation and not to let the administrators do the interpretation, but to be very, very specific if you change this law.

The **Chairman**. Well, I will say this: I think that that is a very persuasive and good statement. I appreciate it personally. I personally do not believe the courts can handle this as well as Members of Congress can, if we will do our jobs. I agree with you that the Congress just loves to write broad, general laws and just throw it out to the bureaucracy, and the bureaucracy just loves to feed on them and create all kinds of regulations that just terrify and scare and ruin the country in so many different ways.

I think we do not do our jobs. I think the regulators overdo their jobs in many cases, and in the process the public loses on both counts.

Mrs. **Foreman**. I assume you are excepting the present company. [Laughter.]

The **Chairman**. I think I have made some real mistakes here myself in the past.

Ms. Haas, you had a comment?

Ms. **Haas**. Yes. I really do not believe that it is correct to characterize the position that the changes being proposed right now are not broad and sweeping changes. When we will move to a system, if we were, to change the definition of "safe" and refine the Delaney amendment in such a way that previously unsafe additives would be considered safe, then that gives consumers a great concern, and rightly so.

I think for that reason our conservative approach has been one that reflects the basic question that I think the Congress must answer: Is the food going to be more safe, just as safe, or not as safe because of the legislation that might occur?

The **Chairman**. Let me thank all of you for coming today. I think this has been an informative and a very delightful panel to listen to. We appreciate the efforts that you put forth.

I would just state this in closing: Over the past three days this committee has heard from more than 12 of our Nation's top scientists, and their cumulative testimony, at least as I view it, expressed a degree of consensus which, frankly, I did not expect. I did not expect there to be that much consensus. They suggest a number of the revisions of the law, particularly modification of the Delaney clause, adoption of the more realistic safety standard, and a provision for consideration of health benefits in the decisionmaking process.

The majority of you argue against those changes. I respect your positions and your right to do so. All I am saying is I have not heard much support elsewhere for those arguments. I am sure there are others who do support you.

In addition of those who have testified thus far on the Monsanto decision, no one would agree with you that Monsanto takes care of food safety problems.

On risk assessment, no other witnesses thought that, used properly, risk assessment would endanger the public health.

I am not saying that none of you have made good points in your testimony. I intend to study your testimony in some detail. I think you have noticed I have listened very raptly to your testimony. I respect your positions, and I respect you as individuals.

Let me also suggest to you that you go back and strongly review what these eminent scientists have been saying the last three days. I think that is important, too.

I think it is important that we do arrive at a consensus to resolve some of these difficulties that are not simple, but are really very big problems in our society today. These laws have not been looked at for 25 years in terms of true congressional review. That is what we are trying to do. Hopefully, we are doing it in a reasonable way.

Again, thank you so much for coming. We appreciate the time you have spent with us today.

Our final panel consists of representatives of various industry groups. We will start with Dr. Howard Roberts, who will testify on behalf of the National Soft Drink Association, where he is vice president for science and technology. Dr. Roberts has also served as Director of the Bureau of Foods with the Food and Drug Administration.

Dr. Sherwin Gardner will follow, speaking as vice president for science and technology for the Grocery Manufacturers of America. Dr. Gardner has served as Deputy Commissioner, then Acting Commissioner, for the Food and Drug Administration.

We will then hear from Mr. Robert Wilmoth, who is the general counsel for Armour and Co., on behalf of the American Meat Institute; followed by Mr. Andrew Ebert, who represents the National Food Processors Association as their vice president for research, development, and quality assurance.

Following Mr. Ebert, we will hear from Mr. Jerome Heckman, general counsel for the Society of the Plastics Industry, Inc.

To conclude, we will hear from Mr. Ritchie Jordan, testifying on behalf of the National Pork Producers Council.

Gentlemen, I am in a real time bind. I know your testimony is extremely important. Again, we will put all of your written statements in the record as though fully delivered, but I would really appreciate it if you could keep your statements down to 5 or 6 minutes at the very most. If I can, I am going to wave a yellow card when you have one minute left. As you noticed, I did not cut off the last panel. A couple of them went better than double their time, but I would like you to try to live within that if you can.

At this point let's turn to Dr. Roberts.

STATEMENT OF HOWARD R. ROBERTS, PH. D., VICE PRESIDENT, SCIENCE AND TECHNOLOGY, NATIONAL SOFT DRINK ASSOCIATION, WASHINGTON, D.C.

Dr. ROBERTS. Thank you, Mr. Chairman.

My name is Howard Roberts, and I am vice president for science and technology of the National Soft Drink Association, which is the national trade association representing the soft drink industry in the United States.

Our association and its members have long been committed to scientifically and technologically sound policies and to effective, reasonable, and up-to-date food safety laws and regulations.

We appreciate this opportunity to present our views on the important subject of modernizing our Nation's food safety laws.

In the more than two decades since the last revision of the Food, Drug, and Cosmetic Act, substantial changes in science, technology, food production, processing, packaging, and consumer needs and expectations have taken place. Over that period the Food and Drug Administration and U.S. Department of Agriculture have attempted to revise their regulations, policies, and practices to conform to contemporary science and technology within the limits imposed by the law.

However, the limits of the flexibility under current law to revise or modernize policies to be consistent with contemporary science and technology are fast being approached.

Without modest but meaningful modernization of certain provisions of our food safety laws, FDA and USDA could be forced to make decisions in certain circumstances that are not based on all the pertinent scientific evidence available and that do not enhance the protection of the public health.

Quite properly, no group has suggested any change in the fundamental principles of current law; that is, that substances proposed for intentional addition to food should be safe and that the manufacturer or other sponsor of such substances should bear the burden of demonstrating safety before that substance is used in food. These basic principles have made the American food supply the safest in the world and have enabled American consumers to have great confidence in the safety of their food. These basic principles have the unqualified support of our association.

As we have seen in these hearings, the need to modernize our food safety laws has been recognized by a variety of diverse groups that have examined the issue in recent years. Notably, virtually every individual— and that includes myself—who has been responsible for implementing the Nation's food safety laws over the last decade has concluded that modernization is needed to introduce flexibility into the law, so that the food safety regulatory decisions are, to quote Dr. Sanford Miller, currently Director of FDA's Bureau of Foods, "the product of scientific judgment and not legal reflex."

The CHAIRMAN. Let me interrupt you at this point. I will give you a few more minutes, but do you feel, as has been characterized, that the suggestions that have been made thus far are intended to weaken the law?

Dr. ROBERTS. Not at all. By no means.

The CHAIRMAN. In other words, the last panel felt that if we take the suggestions of these eminent scientists who have appeared before us, we would be weakening, not strengthening, the law. Now give me your ideas on that.

Dr. ROBERTS. I would suggest, both from the scientific point of view, Mr. Chairman, as well as from my experience as a Director of the Bureau of Foods, that the kind of modernization that Commissioner Kennedy and Commissioner Goyan talked about, and which the other scientific witnesses supported, would enable the agency to focus on the priority issues of risk, and instead of weakening public health protection, would, indeed, increase public health protection.

The CHAIRMAN. What we are saying here is that we are not interested—I am certainly not interested as chairman of this committee, or as a Member of Congress—in weakening the food safety laws of this country. I do not want to have people exposed to risks that they should not be exposed to.

However, what you have just said is that if we can strengthen the laws by recognizing that there have been tremendous technological advances and by utilizing the best science that we have, we are actually going to do a better job of protecting the American population as a whole.

Did I misstate that?

Dr. ROBERTS. No, indeed. As a matter of fact, I thought that in your opening comments on the first day of the hearing, Mr. Chairman, when you used the term "commonsense," you perfectly described what is needed in modern food law. I think from the record that has been built up in this hearing thus far concerning the kinds of changes that we are talking about, if you do in fact look at this from a commonsense point of view, you cannot help but accept the need for modernization. Again, if you look at food safety from a commonsense point of view, providing increased flexibility of the law and thus permitting the regulatory agencies to base their decisions on all of the scientific information which is available, can only increase public health protection and not weaken it.

The CHAIRMAN. If I understand you correctly, you are saying that if we utilize the science and technology that has burst forth upon the scene over the last number of years, certainly the last 25 years since we last examined this issue, it will not only strengthen the law, but will in fact be doing the public a service with regard to food safety. To do otherwise is to continue the idiotic regulatory battling. Is that a fair way of characterizing it?

Dr. ROBERTS. I think that is an excellent characterization. As both the current and former Commissioners have noted, and I am sure my colleague, Mr. Gardner, with whom I have shared a variety of problems over the course of the years at FDA, would agree, one of our greatest difficulties in the agency was not solely a matter of personal anguish; it was a matter of having our scarce resources diverted to issues of low or no priority.

We wished in so many cases that we did not have to, if you will, waste time when there were other much more important issues on which to focus.

The CHAIRMAN. Is it fair to say that you were constantly, as some of the others have intimated, embroiled in controversy that took your valuable time away from doing what you should have been doing? There is only so much money you can put into regulation and into the agencies of Government. If that money is dissipated in almost irrelevant fights and regulatory activity and overregulation and governmental intrusion, in the end you wind up not serving anybody very well. Am I correct in that?

Dr. ROBERTS. That is exactly right.

The CHAIRMAN. Well, that is what I have been getting out of these hearings.

My desire is to do what is right for the American people, not what is right for the soft drink manufacturers or the grocery manufacturers or the so-called consumer groups in America that you hear of from time to time. I want to do what is right with regard to the vast population in this country. I might add that what we do here affects everybody in the world because all the rest of the world relies heavily upon the food safety laws of the United States.

Dr. ROBERTS. I think that is also a very important point.

The CHAIRMAN. I do not mean to keep interrupting you, but I just want to summarize. It seems to me that it is safe to say that every witness basically is concerned about the same thing; that is, good food safety, good rules, good regulations, and having the laws be strong and protecting the public.

I do not think anybody here wants to do anything that will take away protection from the public. I hope that is true of the industry people as you testify.

I think it is safe to say that virtually every health professional who has worked in this area, who has worked for the Government, basically wants to do the same; that is, protect the public.

Am I wrong about that?

Dr. ROBERTS. You are 100 percent correct, Mr. Chairman.

The CHAIRMAN. Go ahead.

Dr. ROBERTS. Thank you.

The CHAIRMAN. I am sorry to interrupt.

Dr. ROBERTS. There are three significant developments in science and technology that I think make our current laws inadequate to resolve current food safety issues in a reasonable, informed, and a socially desirable way.

First of all, our scientific and technical knowledge about the components of the food supply is much broader than it was 25 years ago, and this knowledge makes clear the need to differentiate among risks.

Second, our ability to accumulate useful toxicological information about, and make decisions on, substances in food is far more sophisticated today than it was when the laws were last considered and revised.

Third, reliable techniques are available which enable us to differentiate between risks which warrant regulatory attention and those which do not.

The rigidity of certain provisions of current law, which may well have reflected the state of the knowledge of 25 years ago, should be alleviated to permit contemporary decisions to be made on the basis of fully informed scientific judgment. A law which is inadequate to permit the utilization of contemporary science and technology and which does not allow for scientific progress does not serve the public well.

NSDA supports limited, focused changes in five aspects of current law:

First, the absence of a statutory definition of "safe" for food and color additives has encouraged a drift in regulatory policy toward a zero risk standard, which was not intended by the Congress, cannot be attained, and, moreover, irrationally diverts limited regulatory resources. NSDA considers it essential to adopt a definition of "safe" which retains the reasonable certainty concept but which also recognizes that the concept of insignificant or negligible risk is an appropriate basis for assuring the safety of food.

Second, the inflexibility of the Delaney clause for food and color additives precludes consideration of the degree of risk, if any, posed to humans by a particular substance. The current law thus prevents distinctions from being made on the basis of informed, scientific judgment. NSDA urges this committee to retain the general principle of the Delaney clause but to amend that provision to permit the proponent of use of an additive to demonstrate to the satisfaction of the regulatory agencies that a substance shown to "induce" cancer in animals under a particular set of test conditions is, nevertheless, safe under the intended conditions of human use.

Third, under existing law FDA may not take into account the health-related benefits of an additive in deciding whether its risks are acceptable. NSDA urges this committee to authorize FDA to continue approval of a long-used additive with no practicable substitute, which cannot be authorized for continued use on the basis of a safety assessment alone, when the risks of the additive are acceptable on account of the health benefits.

Fourth, regulatory decisions involving significant scientific issues are more credible when based on the advice and counsel of independent, scientific experts. Although FDA does resort to independent peer review on occasion, current food law does not insure that informed, independent scientific advice is obtained on all important safety issues.

We urge this committee to adopt an independent, scientific peer review provision that will insure that the best scientific advice available is obtained on important food safety issues.

Fifth, the authority of FDA and USDA to provide for the orderly removal of a substance from the food supply, when such removal is warranted, is extremely limited. NSDA urges that the laws be revised to include a provision to authorize a phaseout of the use of such substances.

In conclusion, Mr. Chairman, serious consideration of the need for and objectives of change in our Nation's food safety law has been underway in many quarters for nearly 6 years. Prestigious scientific groups and individual scientists, former senior FDA and USDA officials, industry groups, and numerous others have concluded that modernization is needed.

Without thoughtful, modest, but meaningful, changes in these laws, the credibility of our food safety system will be diminished, limited resources will be misallocated for trivial tasks and innovation in food and food packaging technology will be stifled with little, if any, gain in public health protection.

Revision along the lines discussed in this testimony, on the other hand, will permit this country to retain its enviable position worldwide of having strong food safety laws which insure the safest food supply in the world, while also providing consumers with varied, wholesome, plentiful, and affordable sources of nutrition, sustenance, and enjoyment.

The National Soft Drink Association is pleased to have had this opportunity to contribute to the resolution of these important questions of public policy at these milestone hearings, and we stand ready to assist the committee and the staff in the future consideration of this issue.

Thank you, Mr. Chairman.

[The prepared statement of Dr. Roberts follows:]

STATEMENT

BY

HOWARD R. ROBERTS, Ph.D.

VICE PRESIDENT, SCIENCE AND TECHNOLOGY,

NATIONAL SOFT DRINK ASSOCIATION

ON BEHALF OF THE

NATIONAL SOFT DRINK ASSOCIATION

BEFORE THE

COMMITTEE ON LABOR AND HUMAN RESOURCES

UNITED STATES SENATE

JUNE 10, 1983

Mr. Chairman and Members of the Committee:

My name is Howard R. Roberts and I am Vice President, Science and Technology, National Soft Drink Association. I am pleased to have this opportunity to testify before this Committee on behalf of our industry.

The National Soft Drink Association ("NSDA") and its member companies appreciate this opportunity to present our views on the important subject of modernizing our nation's food safety laws. We commend the Chairman and Ranking Minority Member for their interest in, and commitment to, bipartisan consideration of this issue and for devoting substantial time and effort during these hearings to this matter.

NSDA is the national trade association which represents the soft drink industry in the United States. Approximately seventy-six percent of the nation's 1600 soft drink manufacturers are active members of the Association. These members account for more than 90 percent of the soft drink production in this country. In addition, the vast majority of soft drink franchisers who manufacture the concentrates and syrups from which soft drinks are made are associate members of the Association. NSDA and its members have a longstanding interest in, and commitment to, scientifically and technologically sound food policies and to effective, reasonable, and up-to-date food safety laws and regulations. We are proud to be a major part of this nation's food industry which consistently provides American consumers with the most varied, wholesome, affordable and safe food supply in the world.

I. INTRODUCTION.

Current food safety policy is derived from the provisions of the Federal Food, Drug and Cosmetic Act, 21 U.S.C. § 321 et seq. ("FDC Act"), which is enforced by the Food and Drug Administration, and for meat, poultry and egg products, respectively, the Federal Meat Inspection Act, the Poultry Products Inspection Act, and the Egg Products Inspection Act,*/ which are enforced by the U.S. Department of Agriculture. Major provisions of those Acts first appeared as federal law in 1906. In 1938, the Congress enacted the basic FDC Act which still governs today. Several significant amendments, especially the Food Additives Amendment of 1958 and the Color Additive Amendments of 1960, have been enacted since 1938.

Comprehensive consideration of the food safety provisions of the FDC Act by the Congress has not occurred since 1958. In the more than two decades since, substantial changes in science, technology, food production, processing and packaging, and consumer needs and expectations have taken place. Over that period, FDA and USDA have attempted to revise their regulations, policies and practices to conform to contemporary science and technology, within the limits imposed by the law.

It has become increasingly apparent, however, to the agencies, independent scientific and public policy groups, the food industry and others, that despite these attempts, advances in science and technology have exceeded the limits of the agencies' ability to adapt their policies. The limits of the flexibility under current law to revise or modernize policies to be consistent with contemporary science and technology are being approached. Without modest, but meaningful modernization of certain provisions of our food safety laws, FDA and USDA could be forced to make decisions in certain circumstances that are not based on all the pertinent scientific evidence available and that do not enhance the protection of the public health, but instead inhibit innovation in product and packaging technology. Ultimately, with such unfounded decisions, the credibility of the regulatory process would be diminished in the eyes of the public.

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*/ 21 U.S.C. § 601 et seq., 21 U.S.C. § 451 et seq., and 21 U.S.C. § 1031 et seq.

Quite properly, no group has suggested any change in the fundamental tenets of current law: substances proposed for intentional addition to food should be safe and the manufacturer or other sponsor of such substances should bear the burden of demonstrating safety before the substance is used in food. These basic tenets have made the American food supply the safest in the world and have enabled American consumers to have great confidence in the safety of their food. These basic tenets have the unqualified support of NSDA.

II. THE CONSENSUS FOR MODERNIZATION IS BROAD.

The need to modernize our food safety laws has been recognized by virtually every group that has examined the issue in recent years. Awareness of the need to reexamine our food safety laws and consideration of the areas in need of modernization began in earnest, however, in 1977 when FDA announced its intention to prohibit the use of saccharin, the only approved non-nutritive sweetener. When the Congress passed the Saccharin Study and Labeling Act,*/ not only did it impose a moratorium on efforts to ban saccharin, but it authorized a comprehensive study of food safety policy by the National Academy of Sciences. The Academy's Report**/, issued in 1979, recommends changes in food safety policy to conform it to current scientific knowledge, and administrative and social realities. The Co-chairmen of this report***/ described the imperative of food safety policy as follows:

> Hence, the nation's food safety policy must constitute a reasonable societal framework in which individual consumers, industries and governments can work together with the scientific and medical professions to provide reasonably priced, plentiful, and healthful food. An all-or-none strategy

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*/ Pub. L. 95-203, 95th Cong., November 23, 1977. The moratorium imposed under section 3 of the Act was for an initial term of 18 months. The Congress has consistently extended the term, most recently on April 22, 1983 for another term of 24 months (Pub. L. 98-22).

**/ "Food Safety Policy, Scientific and Societal Considerations," National Academy of Sciences, Institute of Medicine, March, 1979 ("NAS Report").

***/ The panel which prepared the NAS Report was chaired by Walter A. Rosenblith and Clifford Grobstein.

> aspiring to unattainable risklessness has under these circumstances little chance of being effective or successful.*/

These same conclusions, and the need for prudent change in our nation's food safety laws and policies, have been recognized by a diverse group of interests, including the Federation of American Societies for Experimental Biology (FASEB)**/ the Food Safety Council,***/ the FDA, ****/ other federal agencies, scientific groups, many members of the U.S. Congress, members of academia, and a broad spectrum of concerned industry groups. Notably, virtually every individual who has been responsible for implementing the nation's food safety laws over the last decade has concluded that modernization is needed to introduce flexibility into the law so that food safety regulatory decisions are, to quote Dr. Sanford Miller, currently Director of FDA's Bureau of Foods, the product of "scientific judgment, not legal reflex."[*]

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*/ Panel II Chairmen's Preface at xvii.

**/ See, for example, "Insights on Food Safety Evaluation," Federation of American Societies for Experimental Biology," December, 1982.

***/ "Proposed System for Food Safety Assessment," Final Report of the Scientific Committee of the Food Safety Council, June, 1980.

****/ Numerous officials of the Agency, including its Commissioners, have testified on and spoken of the need for increased flexibility in the food safety provisions of the FDC Act. In 1981, the General Accounting Office surveyed nine former FDA Commissioners and General Counsels (among others). Eight of the nine individuals supported changing the Delaney Clause. See, "Regulation of Cancer-Causing Food Additives - Time for a Change?", General Accounting Office, December 11, 1981.

III. ADVANCES IN SCIENCE AND TECHNOLOGY CREATE A NEED AND PROVIDE THE BASIS FOR THE MODERNIZATION OF THE LAWS.

As noted, our nation's food safety laws have not been comprehensively reexamined or revised in over twenty-five years. Although the law has been static, our scientific and technological knowledge and capabilities have changed significantly.

There are three significant developments in science and technology that make our current laws inadequate to resolve current food safety issues in a reasonable, informed, socially desirable way. First, our scientific and technical knowledge about the components of the food supply is much broader than it was twenty-five years ago, and, this knowledge makes clear the need to differentiate between risks. Second, our ability to accumulate useful toxicological information about and make decisions on, substances in food is far more sophisticated today than it was when the laws were last considered and revised. Third, reliable techniques are available which enable us to differentiate between risks which warrant regulatory attention and those which do not.

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[*] Samuel W. Johnson Memorial Lecture, "Food Safety and Public Expectations," presented at the Connecticut Agricultural Experiment Station Plant Science Day, August 11, 1982.

These changes -- in the areas of toxicology, carcinogenesis, animal testing, epidemiology, analytical chemistry, and techniques of risk assessment -- collectively render certain aspects of current law outmoded and thus regulatory decisions that do not embody the best informed scientific judgments of which we are now capable can result. The rigidity of certain provisions of current law, which may well have reflected the state of knowledge twenty five years ago, should be alleviated to permit contemporary decisions to be made on the basis of fully informed scientific judgment. A law which is inadequate to permit the utilization of contemporary science and technology and which does not allow for scientific progress does not serve the public well. Although many of these developments have been addressed in detail by previous witnesses, their importance to the resolution of this issue cannot be overstated, so we summarize them here.

A. Toxicology

Food safety decisions are based on the toxicological data accumulated about a substance from a variety of tests in laboratory animals, other laboratory tests, comparative metabolic and pharmacokinetic studies, epidemiological studies, mathematical models, and biological considerations. The predominant change that has occurred in toxicological testing since the food safety laws were last reexamined relates to the amount of information generated in studies now routinely conducted and the far more sophisticated interpretations of those data that toxicologists are now capable of rendering. For example, in chronic bioassays, we now use more animals and dose levels, pay greater attention to animal diet and care, comply with good laboratory practices, place greater emphasis on auxiliary measurements (*e.g.*, metabolic and physiologic effects) and undertake more comprehensive pathology examinations.

These improvements in study design and conduct provide scientists with information and insights unavailable some years ago, and enable them to better understand, for example, the *reasons* why a particular effect is seen in animals. This information, coupled with data from other new test systems (*e.g.*, short-term tests) permits scientists to evaluate the potential human risk of substances on the basis of differences among different species and particularly between the test animal and humans in such areas as absorption, distribution, metabolism, and excretion, together with differences in the type of end point and/or target organ. Significantly, a much better understanding of toxicity can be gained from current evaluations of the dose/response relationship especially when effects at high doses may be due to a secondary mechanism operating at only those high doses rather than to primary toxicity.

FDA has done much to attempt to accommodate these scientific advances into its regulatory decisions. Nevertheless, the law, in certain instances, does not permit the full scientific inquiry now possible.

B. Analytical Chemistry

Many of the problems of current law stem from the dramatic advances in analytical chemistry over the last twenty-five years. In 1958, analytical methods capable of detecting substances in the parts-per-million range were considered advanced; today, methods routinely detect substances to the low parts per billion range and even to the parts per trillion range.*/ This extraordinary increase in analytical sensitivity enables scientists to identify and quantify the presence in food of natural and unavoidable constituents, trace constituents of food additives and color additives and minute amounts of other substances whose existence in food would heretofore have gone unnoticed. No one could possibly have anticipated this analytical capability when the law was last substantially revised in 1958 and therefore the law was not then designed to permit regulatory officials to exercise sound scientific judgment in deciding whether food constituents present in such small quantities are safe for human use.

It should be emphasized that a food constituent or trace component thereof is not necessarily safe for use simply because its presence in food would not have been detected previously. It is true, however, that the current law was not drafted with the awareness of the presence of minute or trace levels of substances in food. The policies embodied in it, therefore, do not always permit regulators to distinguish between significant risks to human health and those inconsequential, trivial or negligible ones that do not warrant the application of always limited regulatory resources. Since current law may prohibit trace constituents of no toxicological significance, it clearly should be made more flexible.

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*/ One part per trillion is the equivalent of one second in approximately 32,000 years.

C. Carcinogenicity

We have made great progress in our understanding of the carcinogenic process since 1958, although that understanding certainly is by no means complete. Our increased understanding demonstrates that the process is indeed complex and cannot be adequately treated by the same yes-no considerations believed to be adequate in 1958. Current food law does not always reflect the state of current knowledge.

Existing law permits no distinction among animal carcinogens either relative to potency or type.[*] Thus, every animal carcinogen is in effect presumed to present the same risk to humans, a presumption totally at odds with current scientific knowledge. Today, for example, scientists routinely differentiate between genotoxic carcinogens (*i.e.*, those which act directly, or after metabolic conversion, with DNA) and epigenetic carcinogens, those which act as promoters or modifiers. It is also obvious to scientists now that animal carcinogens differ markedly in potency, some by orders of magnitude. Pronounced differences in effects among different species and strains, and even among the sexes of the same strain are often observed. Some carcinogens are associated with specific site effects whereas others are associated with an increase above background at multiple sites. In addition, carcinogens can differ markedly relative to the tumor time of onset. The carcinogenic effects of some compounds may arise from neoplastic transformation dependent on toxicity produced only by sufficiently high dose levels; such compounds would be expected to present little, if any, carcinogenic risk at non-toxic dose levels which might still be considerably above levels of human exposure.

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[*] At the 1982 winter meeting of the Toxicology Forum, Dr. Gary Flamm, Associate Director for Toxicological Sciences, Bureau of Foods, Food and Drug Administration, pointed out that twenty-two different terms had been used during the discussions to refer to "carcinogens." "Proceedings of the Toxicology Forum," February 15-17, 1982 at page 344.

Despite these numerous differences among animal carcinogens and the clear implications they have relative to the assessments of risk to human health, current law and policy do not provide for regulatory decisionmaking which is in accord with the state of science.

D. Food Safety Assessments

Regulatory decision-making on food safety necessarily requires scientists and policy makers to make judgments about the significance of results of tests in animal systems (and epidemological studies, if available) to human health. These safety assessments often involve the extrapolatation from the high doses used in animal experiments to the levels at which humans are expected to consume the substance and the drawing of conclusions about the risks to human health, if any, from such exposure. These assessments, made by regulatory officials worldwide,have been the basis for regulatory decisions in food safety and related situations from the outset of government involvement.

When dealing with non-carcinogenic effects in animals, scientists and regulators have routinely used a "safety factor," such as 1:100, applied to the highest level of exposure of the animals to the test substance at which no effects were detected. The application of the safety factor to this no-observed effect level (NOEL) in turn yields an acceptable daily intake (ADI) for the substance. On the basis of the calculated ADI, a regulatory decision is made about the use of the substance. The use of safety factors is a longstanding safety assessment technique.*/

In recent years, techniques of quantitative risk assessment based on mathematical models and biological considerations have been developed, refined _and_, when the animal model is applicable to humans, relied upon as _part_ of the basis for regulatory decisions in a variety of health and safety areas, including food safety, occupational and environmental exposures and others.**/ Quantitative risk assessment, as one part of a broader food safety assessment process, gives the regulator a frame of reference within which to evaluate the risks of a particular substance to human health. The advantage of quantitative risk assessment over other available techniques is that it provides a systematic basis to analyze various regulatory options, unless, of course, an unattainable "no risk" policy is pursued, in which case distinctions among risks are irrelevant.*/ Informed scientific judgments about the magnitude, if any, of risks from substances in the food supply are far more credible, neutral and justifiable when the decisionmaker is able to obtain an informed sense of the relative ordering of various risks and make the regulatory decision with knowledge of the anticipated upper limit on the risk.**/ If risk assessments are not used as part of food safety decision-making, decisionmakers are open to charges of political bias, the credibility of the decisions with the public and internationally is reduced and governmental and private resources are misdirected toward the elimination of inconsequential risks, while others which may warrant attention are ignored.

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*/ Safety factors are an endpoint assessment tool. That is, the results of the toxicological testing are determined and a safety factor applied to a single end-point (the NOEL). The relationship between the various doses fed test animals and the responses elicited is ignored in this approach.

**/ _See_, _for example_, FDA's decisions involving the color additives, lead acetate (45 _Fed_. _Reg_. 72112, October 31, (1980) and D & C Green No. 6 (47 _Fed_. _Reg_. 14138, April 2, 1982); FDA's advance notice of proposed rulemaking on regulating carcinogenic chemicals in food and color additives, (47 _Fed_. _Reg_. 14463, April 2, 1982); and other examples of the use of risk assessment in regulatory decisionmaking cited in "Application of Risk Assessment to Food Safety Decisionmaking," International Life Sciences Institute, 1983, accepted for publication in Vol. 3, No. 3, September 1983 _Regulatory Toxicology and Pharmacology_.

It is essential that the scientific techniques of quantitative risk assessment not be confused with the policy judgments of risk management. Risk assessment is a valuable tool or aid to decisionmaking. Risk management is the application of risk assessments and other pertinent scientific data and insights to specific substances in the context of laws and policies and the determination of appropriate regulatory strategies to manage, reduce or eliminate risks. The resulting regulatory action can involve severe use restrictions, limited use levels, labeling, or perhaps only good manufacturing practice limitations. Risk management thus involves far more than the mechanical or rote application of a quantitative risk assessment to a particular circumstance; risk management is engaged in daily by our health and safety regulatory agencies, which have increasingly used risk assessment as a tool in carrying out their risk management responsibilities. Modernizing the food safety laws to permit reliance on risk assessments in all food safety decisions will enhance the scientific basis of those decisions and permit FDA and USDA to devise reasonable solutions to regulatory problems, that is, to better manage risks.

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*/ See for example, "Quantitative Risk Assessment In Regulation," ed. by Lester Lave, 1982.

**/ Many of the current issues involving risk assessment are explored in a recent report by the National Research Council, National Academy of Sciences, entitled "Risk Assessment in the Federal Government: Managing the Process," 1983.

IV. SPECIFIC PROPOSALS TO MODERNIZE THE EXISTING LAW.

NSDA supports limited, focused changes in five aspects of current law. These changes will introduce needed flexibility into current law, permit the agencies to base their regulatory decisions on an informed, complete scientific basis, help ensure that regulatory resources are applied efficiently and directed at significant sources of risk, make our food safety laws consistent with those of other industrial nations and the approaches of various international organizations and, to quote the National

Academy of Sciences again, permit all concerned parties to work together to provide a "reasonably priced, plentiful, and healthful" food supply.

Current law would be substantially improved if the following five problem areas were resolved:

- The absence of a statutory definition of safe for food and color additives has encouraged a drift in regulatory policy toward a "zero risk" approach. This "zero risk" policy was not intended by the Congress, cannot be attained, and moreover, diverts limited regulatory resources and attention irrationally.
- The inflexibility of the Delaney Clause for food and color additives which are found to "induce cancer" when ingested by animals precludes consideration of the degree of risk, if any, posed to humans by a particular substance. The current law thus prevents distinctions from being made on the basis of informed scientific judgment.
- Under existing law, FDA may not take into account health-related benefits of an additive in deciding whether its risks are acceptable. For a limited number of long-used, unique substances, such authority, when needed, would ensure regulatory decisions consistent with the rational protection of the public health.
- Regulatory decisions involving significant scientific issues are more credible when based on the advice and counsel of independent scientific experts. Although FDA does resort to independent peer review on occasion, current food law

does not ensure that informed independent scientific advice is obtained on important food safety issues.

- The authority of FDA and USDA to provide for the orderly removal of a substance from the food supply, when such removal is warranted, is extremely limited. As the nitrite episode illustrates, long-used unique substances can present special problems when a decision to eliminate them from food is made. A provision to authorize the agencies to phase-out the use of such substances is needed.

I will now turn to each of these problem areas and NSDA's proposals to resolve them.

A. Definition of "Safe"

Under existing law, food and color additives and other substances intentionally added to food must be shown to be "safe" before they are used.*/ Although the Act currently does not define the term "safe," it has been interpreted by the FDA to mean a "reasonable certainty of no harm" from the substance under its intended conditions of use.**/ "Reasonable certainty" is the degree of confidence in the outcome that the decisionmaker must have; the Congress quite properly recognized in 1958 that

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*/ *See, for example*, section 409(c) of the FDC Act, 21 U.S.C. § 348(c).

**/ This phrase is derived from the reports of the Senate and the House of Representatives which accompanied the Food Additives Amendment of 1958. *See*, *for example*, H. Rept. 2284, 85th Cong., 2d. Sess., Comm. on Interstate and Foreign Commerce, July 28, 1958. FDA has incorporated the phrase into its regulations as well, 21 C.F.R. § 170.3 (i).

"absolute certainty" was neither possible nor feasible. We do not suggest any change in this feature of current law.

Despite attempts by the FDA and USDA to adapt policy to advancing science, the "no harm" component of the current interpretation of "safe" has led in recent years to a drift in regulatory policy to a "zero risk" standard in which substances are prohibited even though the potential risks from their use are negligible, trivial or insignificant.*/ The drift toward a "zero risk" approach is due, in part, to the influence of the absolute nature of the Delaney Clause and to the absence of a definition of safe in the law itself. The Congress, however, never intended that the concept of zero risk be embodied into the law: the concept is unattainable as a matter of science, and, the pursuit of "zero risk" does not enhance, and indeed may detract from, the protection of the public health.

NSDA considers it essential to adopt a definition of safe which retains the "reasonable certainty" concept but which also recognizes that the concept of "insignificant" or "neglible" risks is an appropriate basis for assuring the safety of food.

B. Delaney Clause

The current absolute Delaney Clause prohibits the exercise of sound, informed scientific judgment on whether an additive found to "induce cancer" when ingested by animals presents a risk of cancer to humans.[*] This rigid, unscientific approach could lead to unnecessary bans of, and refusals to approve, additives which are safe for human use. For example, an additive which contains a trace constituent which is an animal carcinogen, even though the additive itself is not carcinogenic, could be prohibited under the Delaney Clause, without regard to the risk, if any, to humans under the intended conditions of use. Likewise, an additive which "induces cancer" in an animal test but which, because of physiological or other factors, presents, at most, only a theoretical or trivial risk of cancer to humans would be banned.

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*/ See, for example, FDA's discussion of this point in "Policy for Regulating Carcinogenic Chemicals in Food and Color Additives: Advance Notice of Proposed Rulemaking," 47 Fed. Reg. 14463, April 2, 1982.

It is not sound public policy to misapply resources in this way nor is the protection of the public health enhanced by prohibiting additives which pose no genuine public health or safety concern. Since we have the scientific basis to distinguish between additives which present, at most, negligible or insignificant risks of cancer to humans and those that present greater risks, we should conform the policy of the law to the state of our scientific and technological capabilities.

NSDA urges this Committee to retain the general principle of the Delaney Clause. However, consistent with our recommendation on the definition of safe, we consider it essential to amend that provision to permit the proponent of use of an additive to demonstrate to the satisfaction of the regulatory agencies, that a substance shown to "induce" cancer in animals under a particular set of conditions is nevertheless safe under the intended conditions of human use.

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[*] The FDC Act contains three Delaney Clauses: one in section 409(c)(3) applies to food additives; one in section 512(d)(1)(H) to animal drug residues; and the one in section 706(b)(5)(B) to color additives, 21 U.S.C. §§ 348(c)(3), 352(d)(1)(H), and 376(b)(5)(B).

C. Health Benefit Consideration

Concerns in 1977 about saccharin, followed a few years later by concerns about nitrites, and more recent concern with the antioxidant BHA, illustrate the need to authorize FDA to take into account, in special cases, and before it decides to ban a substance, the risks to health presented by an additive and the benefits to health from use (or increased risks from nonuse). If the risks from the use of a substance are acceptable on account of the health benefits -- such as the effects of the additive on the nutritional value of food, use to preserve food, or use for dietary management -- its continued use should be authorized.

Comparing health risks and health benefits is a difficult task and ought not to be a routine part of the food additive review process. When an additive has a long history of use (and thus its risks and benefits are likely to be reasonably ascertainable) and there is no reasonably practicable substitute for it (that is, the benefits cannot be attained through the use of an alternative substance), however, it is appropriate to authorize FDA to undertake the comparison. We do not envision that FDA would need to resort to this authority very often. If it had the authority, however, it would be able to resolve administratively problems presented by this special class of additives.

NSDA urges this Committee to authorize FDA to continue approval of a long-used additive with no practicable substitute which cannot be authorized for continued use on the basis of a safety assessment alone, when the risks of the additive are acceptable on account of the health benefits.

D. Independent Scientific Peer Review

It is widely recognized that if food safety decisions are to be scientifically sound, reliable and credible, the nation's best scientific expertise should be brought to bear on them. FDA recognizes that in some cases it is appropriate and desirable to obtain the expert advice of scientists who are not regular full time employees of the government. In fact, in many areas of its responsibility -- new drug regulation for example -- FDA has rountinely obtained expert advice from outside the agency. And, on occasion, FDA has solicited such advice on food safety scientific issues.

Public credibility and scientific reliability would be enhanced, however, if the law mandated independent scientific review on important food safety issues.[*] Specifically, "peer review" of this sort should: (a) occur early in the regulatory process, so that controversy and concern are not generated without cause; (b) be independent of the agency, by, for example consisting of a standing or ad hoc advisory committee of outside experts; (c) permit interested members of the public to submit pertinent information bearing on the issues before the committee; (d) be limited to a review of the scientific issues involved in the decision so that the decisionmaking responsibility is unequivocally retained with the agency; (e) be advisory to the agency and not binding since ultimate responsibility for the decisions rests with FDA and its expert scientists and policy makers; and (f) be limited to cases in which the scientific issues raised by a particular substance are substantial and peer review can therefore aid in their resolution; referral to the committee should not be mandated in routine cases.

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[*] The National Research Council recently recommended greater use of peer review by FDA's Bureau of Foods, concluding, among other things, that "[I]ndependent scientific review of agency risk assessments improves the scientific quality of the assessments and strengthens them against later challenge." "Risk Assessment In The Federal Government: Managing the Process," at page 144.

NSDA urges this Committee to adopt an "independent scientific peer review" provision that embodies the principles delineated above.

E. Flexibility To Conduct Phase-Outs

Some substances in food that have been in use for a long period of time and which are "unique" -- that is, there are no practicable substitutes readily available which will permit the continued availability of a food or class of foods -- may be found not to satisfy the safety requirements under the Act. As the ongoing process of food safety evaluation continues, it is probable that under current law, an important food constituent may occasionally have to be prohibited.

This situation nearly occurred in the nitrites episode. In that instance, both FDA and USDA quite properly recognized that an immediate ban on the use of nitrites would, in all probability, deprive consumers of a wide variety of foods to which they had become accustomed and on which they relied, expose the consuming public to an increased risk of botulism, and impose significant costs on the food industry. The two agencies also recognized that protection of the public health did not require an immediate ban and so they sought to develop administratively a plan for such a phase-out. This effort was aborted, however, when the Attorney General concluded that a phase-out could not lawfully be conducted under current law.*/ In response to that decision, the Carter Administration proposed legislation to authorize a phase-out.**/

That particular legislative effort was ended when the scientific basis underlying the decision to eliminate nitrites was revised and the continued safe use of nitrites confirmed. Nevertheless, the episode pointed out the need for an administrative mechanism and flexibility to handle such situations.

A phase-out provision should permit the agencies to adopt, by regulation, a schedule for the gradual elimination of a long-used food constituent for which there is no reasonably practicable substitute. In other instances, current law permits the agencies to provide for an orderly change in ingredient use. A phase-out might well provide for the phased reduction of the quantity of use of a substance, or a phased reduction of the types of foods in which it can be used (e.g., substitutes may become available for one use of a substance before others). In deciding on the conditions of a phase-out, the agencies should be authorized to consider all relevant factors, including the health effects related to the use of the substance, the consequences of prohibiting use, the extent to which practicable substitutes are available, and the effects of prohibiting use on the cost and availability of food. It is important that in deciding how to implement a decision to ban a substance, as opposed to the decision on whether to ban it, consideration be given to the economic effects. There is no sound public policy which is served by unnecessarily imposing costs on food processors and increasing the cost of food through the hasty elimination of an important food constituent. Protection of the public health should remain the paramount responsibility of the agencies but its pursuit in those cases where a phaseout is appropriate, ought not to occur without also considering the full range of consequences from the decision to ban.

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*/ Opinion of the Attorney General, March 30, 1979.

**/ S. 886, 96th Cong. 1st Sess., April 5, 1979 and H.R. 3364, 96th Cong. 1st Sess., April 2, 1979.

Finally, any phase-out provision should allow for an adequate period to develop and test substitutes and to provide for their orderly introduction into food. Each phase-out will, of course, be unique. If these matters are to be resolved administratively, however, the regulatory agencies should have ample discretion and authority to structure a phase-out consistent with their best judgment about the balance that should be struck among the competing factors which are to be considered.

NSDA urges this Committee to adopt a phase-out provision consistent with the objectives described above.

V. CONCLUSION.

Serious consideration of the need for, and objectives of, change in our nation's food safety laws has been underway in many quarters for nearly six years. Prestigious scientific groups and individual scientists, former senior FDA and USDA officials, industry groups, and numerous others have concluded that modernization is needed. Without thoughtful, modest, but meaningful changes in these laws, the credibility of our food safety system will be diminished, resources misallocated to trivial risks, and innovation in food and food packaging technology stifled, with little, if any, gain in public health protection. Revision along the lines discussed in this testimony, on the other hand, will permit this country to retain its enviable position worldwide of having strong food safety laws which ensure the safest food supply in the world while also providing consumers with varied, wholesome, plentiful and affordable sources of nutrition, sustenance and enjoyment.

The National Soft Drink Association is pleased to have had the opportunity to contribute to the resolution of these important questions of public policy at these milestone hearings. We stand ready to assist the Committee and staff in its future consideration of this issue.

The CHAIRMAN. Thank you, Dr. Roberts.

We will turn to Dr. Gardner at this point, representing the Grocery Manufacturers of America. He has also served as Deputy Commissioner, then Acting Commissioner, for the Food and Drug Administration.

We welcome you before the committee.

STATEMENT OF SHERWIN GARDNER, VICE PRESIDENT, SCIENCE AND TECHNOLOGY, GROCERY MANUFACTURERS OF AMERICA, INC., WASHINGTON, D.C.

Mr. GARDNER. Thank you, Senator Hatch.

I might correct the record just a bit even before I start. It is simply "Mr." Gardner, not "Dr." Gardner. I have not earned that title yet.

Mr. Chairman, I am Sherwin Gardner, vice president of science and technology of the Grocery Manufacturers of America. GMA is the trade association representing the leading manufacturers of food and other grocery products sold in retail outlets throughout the United States. Our member companies employ over 2.5 million people and have total annual sales in excess of $200 billion.

We appreciate the opportunity to testify before the committee this morning on the important issue of food safety policy, and thank you, Senator Hatch, for the leadership role you have taken on this issue.

The United States has available to it today the safest, most diverse, and most abundant food supply in the world. The safety of our food has been assured by the efforts of food producers and processors and also of the regulatory agencies. The food industry is proud of its safety record and is committed to maintaining it.

The food safety laws of this country have made a remarkable contribution to public health and safety. GMA believes, however, that scientific capability has increased dramatically since their enactment. Accordingly, today our science has far outstripped our law and, therefore, to accommodate advances in science, the current law needs to be modernized.

Testimony already given during the previous two days by former Commissioners and by scientists who made these points with great eloquence and in greater detail acknowledged the need for a change in the law.

GMA advocates three principles we believe are essential to meaningful food safety reform.

The first of these is that food safety policy must differentiate between significant and insignificant risks and must embody insignificant risk as the safety standard. That is, if risk assessment procedures determine that any risk from a food substance is insignificant, that substance should not be prohibited from use.

The second principle we recommend is that food safety policy must provide administrative flexibility in enforcing the law by permitting the use of substances that may not satisfy the insignificant risk standard under two conditions.

First, that they have a long history of use in food and, second, that there be no practicable substitute. Other than these criteria, it is neither necessary nor desirable to provide any other kinds of benefit tests to be administratively applied by USDA or FDA.

The third principle we recommend for food safety reform is that food safety policy continue to reflect the special status of food components of long-established and recognized history as part of our diet. The current GRAS, generally recognized as safe, and prior sanction provisions of the Food, Drug, and Cosmetic Act serve this purpose well and should remain unchanged. In effect, these provisions are a priority-setting mechanism that helps to focus attention and valuable public and private resources on the most important safety concerns.

Despite suggestions to the contrary, GRAS and prior sanction substances are subject to scientific evaluation and may also be subject to regulatory control by FDA and USDA if new scientific information renders them suspect.

Effective food safety regulation requires differentiation among varying levels of risk. GMA supports a risk assessment approach that is relevant to human safety for regulation of the Nation's food supply.

Risk assessment is the essential element of food safety reform. As others have already testified, it is a recognized technique for scientifically and objectively evaluating risk in order to distinguish insignificant from significant and has received increasing use by Federal regulatory agencies. It is a technique that is clearly applicable to all food safety decisions. Incorporation of risk assessment in the act would establish a systematic means to distinguish objectively among risks and to avoid regulating insignificant ones. Its use is one way of assuring objective and consistent food safety decisions.

Mr. Chairman, we appreciate the opportunity to appear before the committee this morning, and we will be pleased to respond to your questions.

[The prepared statement of Mr. Gardner and responses to questions asked by Senators Hatch and Grassley follow:]

Testimony on
Food Safety Policy

Before the

Senate Labor and Human

Resources Committee

June 10, 1983

Food Safety Hearings

Presented by

Sherwin Gardner

Vice President, Science & Technology

Grocery Manufacturers of America, Inc.

June 10, 1983

Mr. Chairman, I am Sherwin Gardner, Vice President, Science and Technology, of the Grocery Manufacturers of America, Inc. (GMA). GMA is the trade association representing the leading manufacturers of food and other grocery products sold in retail outlets throughout the United States. Our member companies employ over 2.5 million people and have total annual sales in excess of $200 billion.

We appreciate the opportunity to testify before the Committee this morning and thank you, Senator Hatch, for the leadership role you have taken on the issue of food safety reform.

GMA is deeply interested in the food safety provisions of the Federal Food, Drug, and Cosmetic Act--and the parallel provisions of the Federal Meat Inspection Act, the Poultry Products Inspection Act, and the Egg Products Inspection Act--that regulate the safety of food ingredients and ultimately the food products that are marketed to consumers.

The United States has available to it today the safest, most diverse, and most abundant food supply in the world. The safety of our food has been assured by the efforts of food producers and processors and of the regulatory agencies. The food industry is proud of its safety record and is committed to maintaining it.

The food safety laws of this country have made a remarkable contribution to public health and safety. GMA believes, however, that scientific capability has increased dramatically since their enactment. Accordingly, today our science has far outstripped our law and therefore, to accomodate advances in science, the current law needs to be modernized.

GMA's committment to food safety reform can be seen in our testimony before the House Committee on Agriculture in September 1980 and our August 1981 petition with the Federal Food and Drug Administration (FDA). Both statements are submitted for the record.

In our statements, then as now GMA advocates principles we believe are essential to meaningful food safety reform. These principles are:

- Food safety policy must differentiate between significant and insignificant risks and must embody insignificant risk as the safety standard. That is, if risk assessment procedures determine that any risk from a food substance is insignificant, that substance should not be prohibited from use.

- Food safety policy must provide flexibility by permitting the use of substances that do not satisfy the insignificant risk standard if they have a long history of use in food and no practicable substitute. Regulatory decisions that apply this policy must be based on broad considerations of public health and consumer benefits, and not restricted to narrow considerations of health benefits of particular food products.

- Food safety policy must continue to reflect the special status of food components with a long established and recognized history as a part of our diet. The current GRAS and prior sanction provisions of the

> Food and Drug and Cosmetic Act serve this purpose well and should be maintained unchanged. In effect, these provisions are a priority-setting mechanism that helps to focus attention and valuable public and private resources on the most important safety concerns.

At the heart of food safety reform is the need to amend the current law and its interpretations to be contemporary with modern science. Current regulatory doctrine requires the banning of any food additive found to induce cancer in test animals at any level of exposure. This requirement overlooks scientific advances which have greatly increased the power of testing for identifying animal carcinogens and which allow for detection of infinitesimal traces of carcinogens posing insignificant risk to humans. This continued adherence to a zero-risk standard is neither practical, feasible nor necessary.

Effective food safety regulation requires differentiation among varying levels of risk. The food supply is replete with risks of all magnitude; a zero-risk food supply is an impossibility. Risk assessment is essential to distinguish between insignificant and significant risks in order to target food safety regulation in an effective manner. GMA supports a risk assessment approach to the regulation of the nation's food supply.

Many essential substances including vitamins (vitamins D_2, A), minerals (selenium) and some amino acids (tryptophan) present varying levels of risk. Common food ingredients have been found to be carcinogenic when fed at high levels to laboratory animals. Such ingredients include substances found naturally in such foods as mustard and strawberries. By their overwhelming response to the proposed ban of saccharin, American consumers and the Congress indicated a willingness to tolerate some degree of risk in some foods for reasons unrelated to health, including pleasure and taste.

Food safety reform must embody insignificant risk as the safety standard. A substance for which there is a reasonable certainty of insignificant risk under intended conditions of use should be deemed "safe".

The term "insignificant risk" has been interpreted in administrative and judicial law as not requiring a zero risk standard. The GMA petition discusses this extensively. We suggest, therefore, that a statutory definition of safe be "a reasonable certainty that the risks of a substance under intended conditions of use are insignificant." This standard needs to be applied uniformly to the Act.

For a substance which presents more than a reasonable certainty of insignificant risk, but has a long history of food use in the United States and for which no practicable substitute exists, a tolerance for its continued use should be provided which is adequate to protect the public health. Food safety reform that adopts this principle would assure that all benefits to consumers, including those of taste and enjoyment, would be considered when a substance does not satisfy the insignificant risk safety standard.

Risk assessment is the essential element of food safety reform. It is a recognized technique for scientifically and objectively evaluating risk in order to distinguish insignificant from significant, and has received increasing use by Federal regulatory agencies. It is a technique that is clearly applicable to all food safety decisions. A report on risk assessment prepared last March by a committee of the National Academy of Sciences identified ways in which the technique could be made more effective.

The NHS Committee described risk assessment as the characterization of the potential adverse effects of human exposure to environmental hazards and comprising a number of scientific analyses, both quantitative and qualitative in nature. The Committee also distinguished between risk assessment and risk management--the former being a scientific process, the latter a regulatory decision making process. We agree with these decisions as stated in our comments to the Committee in February 1982 during its deliberations. A copy of our comments is provided for the record.

Incorporation of risk assessment in the Act would establish a systematic means to distinguish objectively among risks and to avoid regulating insignificant ones. Its use is one way of assuring objective and consistent food safety decisions.

We appreciate the opportunity to appear before the Committee this morning and would be pleased to respond to your questions.

DR. GARDNER

ADDITIONAL QUESTIONS FOR INDUSTRY PANEL PREPARED BY SENATOR HATCH

1) During the hearing, several witnesses discussed the effect of current law on innovation. In your opinion, does current law stifle innovation? How? Please provide examples to support your conclusion?

ADDITIONAL QUESTIONS FOR MR. GARDNER PREPARED BY SENATOR GRASSLEY

1) Having served as Deputy Commissioner of FDA under four commissioners for almost a decade, what is your interpretation of the Administration's definition of "safe"?

2) Would you please elaborate on your statement that health benefits are not the proper criteria for risk benefit analysis.

RESPONSE TO SENATOR HATCH'S QUESTION

1. Current law (the Food Drug and Cosmetic Act) does stifle innovation in several respects.

First, the highly conservative zero-risk doctrine of current regulatory practice establishes equally conservative standards for investment in new product ventures. There is little incentive to invest the enormous amount of resources--skilled scientists and laboratory facilities as well as time and money--in high risk development projects. It is not possible to identify examples of products not undertaken for this reason. However, the case of irradiation processing serves to illustrate the point. Considered a food additive under current law, irradiation processing can provide a means of preservation frequently accomplished by the use of chemical or heat sterilization process. It has the advantages of no exposure to chemical residues, and improved palatability. Much of the development work was accomplished by the U.S..Army Quartermaster Corps and has been carried on for almost 25 years. It is only recently that FDA has given consideration to permitting the use of irradiation processing, and then only for limited use.

Second, the zero-risk doctrine results in extensive and excessive safety testing of new products and processes. It produces a characteristically slow and cautious approach by FDA before approval of a new product. Careful and comprehensive evaluation by the Agency is certainly called for by its public health responsibilities, but when carried to excess the evaluation process can stifle innovation. Thus, when the evaluation process is overly prolonged, it delays the introduction of new products and corresponding recovery of investment. Dr Goyan gave as an example of this the use of asceptic packaging.

Finally, the application of the current law results in continuing evaluation and re-evaluation of previously approved substances. This results in the diversion of scarce and valuable resources for additional testing; many of these are the same kinds of resources that could be used for new product development. A revised food law would lend better balance and selectivity to the re-evaluation of previously approved food substances.

SENATOR GRASSLEY RESPONSES

1. During my service as Deputy Commissioner of FDA the agency interpretation of the term "safe" was, as noted frequently in the record, "a resonable certainty of no harm." In practice this resulted in the non-approval of substances about which there was even the slightest risk or question of risk; the emphasis on the definition was on the term "no harm", and particularly so in the case of suspect carcinogens.

   This position was an application of the view expressed during legislative hearings leading to the 1958 food additives amendments. At that time, the administration interpreted the Delaney Clause prohibition against carcinogens as superfluous; it stated that the general safety clause was sufficient to ban the use of substances that were suspected of causing cancer in man or test animals. Thus, although the FDA proposed to ban saccharin on the basis of the Delaney Clause, it held that saccharin would be banned under the general safety provisions of the Act as well. In another instance, Red No. 2 was banned because it had not been shown to be safe; the results of animal tests raised the question of whether or not Red No. 2 caused cancer.

   Thus, the definition proposed by the Administration's Working Group, in my opinion, would not clearly establish a change in policy--the term "no harm" has a regulatory history giving it the practical meaning of zero risk. A definition of safe without the term no harm, and expressed as a reasonable certainty of insignificant risk or of negligible risk, would clearly establish the necessary non-zero risk policy.

2. The term "health benefits" is one that is subject to widely differing definitions. Some definitions are broad and include such factors as consideration of the availability of food; other definitions are narrow and would apply only to direct health benefits to individuals. This variation in defining and measuring health benefits will only add complexity and controversy to the already difficult scientific process of evaluating risk.

   Nevertheless, Health benefit, however defined, is too narrow a view of the role food plays in our society. There are few substances, aside from essential vitamins and minerals, that are essential to human health. Some foods are consumed solely for pleasure; others are part of a "menu" that make foods palatable and enjoyable when consumed together; still others provide variety in our diets, convenience and out-of-season availability. Viewed solely from a utilitarian health benefit perspective, therefore, some of these other benefits could be lost.

   It should be possible to provide consideration of broad consumer benefits while at the same time establishing controls that will protect public and individual health. As an example, section 406 of the Food Drug and Cosmetic Act now does this for some food substances that are unavoidable or required in production.

   There are two ways to achieve broad benefit consideration in regulating food. One way is for the Congress to make value judgments about the benefits of broad categories of food substances and establish general rules for controling these. This, in effect, is what exists in the different food categories established by the current Act. This approach requires administrative determination of risk by FDA but not of benefit.

   A second way of achieving broad benefit consideration is to authorize the FDA to make the determinations that food substances are required for production or are unavoidable in production--in effect, extending the existing provision of section 406 to substances having a long history of use in food in the United States and no practicable substitute. This approach would preserve important features of our food supply but guard against wholesale introduction of new substances that may present new and additional risks to consumers.

SG/et

The CHAIRMAN. Thank you, Mr. Gardner. We appreciate that.

We will turn to Mr. Wilmoth at this time, who is general counsel for Armour and Co., appearing here on behalf of the American Meat Institute.

STATEMENT OF ROBERT WILMOTH, ASSOCIATE GENERAL COUNSEL, ARMOUR AND CO., REPRESENTING THE AMERICAN MEAT INSTITUTE

Mr. WILMOTH. Thank you, Mr. Chairman.

My name is Robert Wilmoth. I am associate general counsel for Armour and Co. As counsel to Armour, I am responsible for the firm's regulatory compliance, which includes assuring that only safe food ingredients are used in our products.

Before joining Armour, I served in the Office of General Counsel for the Food and Drug Administration, as a trial attorney, and as special assistant to the chief counsel. As a result, for the past 14 years I have worked directly with the regulation of food substances under our current food safety laws.

I am testifying today on behalf of the American Meat Institute. The AMI is the Nation's oldest trade association, representing large and small meat packers and processors. The meat industry is very proud of its products and of its exceptional record that it has built since 1906 in producing safe and wholesome food products that American consumers have come to enjoy and consider an important part of their diet.

The combination of industry quality control and the most comprehensive regulatory scheme faced by any industry has made this possible. We are under no circumstances interested in weakening our food safety law. Safety is and shall remain the No. 1 priority of the meat industry.

It is important that these laws protect the consumer without threatening the integrity of the food supply or the public confidence in the safety and wholesomeness of food. Although the current laws maintained this balance quite effectively for decades, events in recent years, coupled with advancements in science and technology, have shown that some of the basic concepts of our current food safety laws no longer represent sound and responsible public policy.

During the last few days this committee has heard a great deal about the abilities of today's scientists to identify toxic substances in minute quantities. Respected scientists have explained the extent to which we can extrapolate animal test results and assess the potential risk that a substance might present to human health under its intended conditions of use.

We believe that the Nation's food safety laws must be modernized to recognize these scientific advances.

The meat industry, Government regulators, and the American consumer learned the hard way just how out of step our contemporary science and current laws can be.

In August 1978, FDA and the U.S. Department of Agriculture jointly announced that a study conducted at the Massachusetts Institute of Technology indicated that sodium nitrite caused cancer in laboratory animals. Sodium nitrite has been used for centuries as a preservative in meat and poultry products to prevent the deadly food poison, botulism. With no known substitute for the preservative, the agencies hope to avoid the automatic ban of the substance demanded by law, seeking instead to eliminate nitrite from the food supply gradually.

However, the Department of Justice concluded that a phaseout was not authorized under current law. It was finally an independent review of the MIT study that raised serious questions about the scientific reliability of the nitrite study and ultimately led agencies to reject the study's conclusion.

The problem under scrutiny by this committee is not the concern of the fundamental safety of the food supply. America is fortunate to have the safest and most wholesome food supply in the world. The problem concerns how much longer the laws can remain unchanged without serious interruption of major segments of our food supply.

We believe that the following elements must be included in an immediate revision of the law which governs our food supply:

First, the definition of "safe" must be included. Under current law the term "safe," while not specifically defined, has been determined to mean a reasonable certainty of no harm. This term, when applied to various substances, has resulted in a no risk approach by the agency. Provisions of our food safety laws must clearly mandate that Congress does not intend our food supply to be governed by a no risk standard but rather one which is governed by an insignificant risk standard.

Second, the need to consider benefits of a substance in the food supply must be mandated. The law must recognize that although the substance might present some risk, there are situations where the benefits that it offers consumers make its continued availability important. There are substances such as nitrites that perform extremely important functions in food safety in terms of preservation and prevention of the deadly botulism toxin.

Third, phaseout permission should be included. Federal agencies should be authorized to permit the gradual elimination from the food supply, under limited circumstances, of substances with long histories of safe use for which their exists no substitutes and the prohibition of which would adversely affect the entire Nation's food supply.

As was clearly demonstrated by the nitrite experience, phaseout authority represents one of the most pressing needs in the area of food safety law reform if massive disruptions in the Nation's food supply are to be avoided.

Finally, the agency's decisionmakers should be directed to submit and subject all available data concerning the suspect substance to a scientific review by qualified experts independent of agencies involved before using such data as the basis of regulatory action. Peer review by scientists independent of the agency should help insure that current scientific procedures are followed and that the Government, industry, and the American consumer are all competent in the food safety decisions that are to be made.

The nitrite experience taught us all, including Members of Congress, a great deal about the Nation's food safety laws. In April 1981, an article in the Washington Post Mazagine about the nitrite episode explored the problem being presented to you this week. It is the story of how regulators, with the best intentions, felt compelled to condemn one-tenth of America's food supply. Explaining the dilemma facing the decisionmaker, the author pointed out, "If the regulator goes slowly, he can be accused of covering up what he already thinks he knows, of being a tool of the business interest he is supposed to regulate. If he moves too quickly, he can be accused of wrecklessly toying with people's jobs, of needlessly damaging the industry and economy."

In short, the nitrite episode represented a classic conflict between the outdated public policy and contemporary science. It taught us, as most of the witnesses have testified before me, the time has come to modernize the laws to reflect the public policy that allows science to advance with jeopardizing segments of the American food supply.

Thank you very much.

[The prepared statement of Mr. Wilmoth follows:]

Statement

By

Robert Wilmoth

Associate General Counsel

Armour and Company

On Behalf of the

American Meat Institute

Before the

Committee on Labor and Human Resources

United States Senate

June 10, 1983

Mr. Chairman and Members of the Committee:

My name is Robert Wilmoth. I am Associate General Counsel of Armour and Company. Armour's subsidiaries, Armour Food Company and Armour-Dial, Inc., produce and distribute across the nation more than $2.3 billion worth of fresh, processed and shelf-stable meat and poultry food products. As Counsel to Armour, I am responsible among other things for the firm's regulatory compliance efforts which include assuring that only safe food ingredients are used in our products. Before joining Armour, I served in the Office of the General Counsel of the Food and Drug Administration as a trial attorney and Special Assistant to the Chief Counsel. As a result, for the past fourteen years I have worked directly with the regulation of food substances under our current food safety laws. I am pleased that this Committee has taken the initiative in reviewing those laws and considering ways to bring them into step with modern science.

I am testifying today on behalf of the American Meat Institute (AMI). I serve on the Institute's Legal Committee, which I chaired for two years. AMI is the nation's oldest trade association representing large and small meat packers and processors. The Institute has approximately 330 members throughout the country. More than 120,000 people are employed by these companies; 70% of AMI's members employ fewer than 100 people. AMI has been representing the meat industry since the safety and wholesomeness of meat products first became regulated by the Federal government in 1906.

Introduction

It is important that our food safety laws protect the consumer without threatening the integrity of the food supply or the public confidence in the safety and wholesomeness of food. Although the current laws maintained this balance quite effectively for decades, events in recent years, coupled with advancements in science and technology, have shown that some of the twenty-five year old concepts embodied in our current food safety laws no longer represent sound and responsible public policy. Accordingly, AMI believes that these laws should be reviewed carefully and revised in a few limited but fundamental respects.

The meat industry is very proud of its products and the exceptional record that it has built since 1906 in producing safe and wholesome food products that American consumers have come to enjoy and consider to be important to their diet. A combination of industry quality control and the most comprehensive regulatory scheme faced by any industry has made this possible.

Our safety record speaks for itself. The problem under discussion today does not concern the fundamental safety of the food supply, but the laws under which that food supply is regulated.

Innovations in agriculture and processing during this century have transformed the American food supply from a relatively simple product of local farming and home preparation to a wide variety of processed products. The meat industry works continually on new product research and development in order that we may offer our customers safe, wholesome and enjoyable products at the lowest possible prices. This is in response to the needs and demands of our consumers as their lifestyles have changed with our constantly changing society. It is critical that the laws which seek to ensure the safety of food recognize the scientific advances made in food technology and processing and accommodate, rather than inhibit, those advances.

Under no circumstances should our food safety laws be weakened. Safety is and shall remain the number one priority of the meat industry. At the same time, we must be certain that our laws permit regulators to make rational and scientifically sound judgments, and do not -- in "knee jerk" fashion -- force removal from the marketplace of safe foods and safe food ingredients that provide very important benefits to consumers.

Meat Industry Experience

The meat industry and the public learned the hard way just how out of step with contemporary science the current laws can be in August 1978. It was then that FDA and the U.S. Department of Agriculture (USDA) jointly announced that a study conducted at the Massachusetts Institute of Technology (MIT) revealed that sodium nitrite had been shown to cause cancer in laboratory animals. The agencies, which have some overlapping and parallel regulatory responsibilities with respect to meat products and food additives, stated that they intended to ban nitrite from the food supply. Sodium nitrite derived from sodium nitrate had been used directly or indirectly as a preservative in meat and poultry products for many years to prevent the deadly food poison botulinum toxin; there was no known reasonably practicable substitute for the preservative, so the agencies hoped to avoid an immediate and automatic ban of the substance, seeking instead to eliminate nitrite from foods gradually.

You certainly will recall the nationwide controversy that followed the dramatic FDA/USDA nitrite announcement. The debate, however, did not focus initially on the validity of the MIT study. Instead, argument centered on how quickly the agencies would have to ban nitrite and the extent to which either agency was legally allowed to phase it out of the food processing system. The United States Department of Justice ultimately concluded that such a phase-out was not authorized under current law.

Only after release to the public of the MIT study, did FDA initiate an independent review of that study. The independent review raised serious questions about the scientific reliability of the MIT study and ultimately led the agencies to reject their initial conclusion about sodium nitrite's safety and to give nitrite a "clean bill of health." By the way, it was only after several Members of Congress objected to the agencies' total reliance on only one study which, without verification or duplication, could not be considered conclusive, that the study was subjected to peer review by scientists outside the agencies involved.

The nitrite experience taught regulators and Members of Congress a great deal about the nation's food safety laws. In an April 1981 article in the Washington Post Magazine, the nitrite episode was explored as a story of how regulators, with the best of intentions, felt compelled to condemn one tenth of the American food supply. Explaining the dilemma facing the decision-maker, the article pointed out that, "If the regulator goes slowly ... he can be accused of covering up what he already thinks he knows ... of being a tool of the business interests he is supposed to regulate ... If he moves too quickly, he can be accused of recklessly toying with people's jobs, of needlessly damaging industry and the economy..."

In short, the nitrite episode represented a classic conflict between outdated public policy and contemporary science. It taught us that the time had come to modernize the laws that reflect that public policy.

Recommendations for Change

During the last few days, this Committee has heard a great deal about the abilities of today's scientists to identify toxic substances in minute quantities. Respected scientists have explained the extent to which we can extrapolate animal test results and assess the potential risks that a substance might present to human health under its intended conditions of use. The nation's food safety laws should be modified to accommodate these advances. Among the elements that should be included in a revision of the laws are the following:

- In deciding whether or not a food substance is "safe," agencies should examine all available data, and assess the extent to which a suspect substance presents risks to human health;

- the law must recognize that, although a substance might present some risk, there are situations where the benefits that it offers consumers make its continued availability important;

- Federal agencies should be authorized to permit the gradual elimination from the food supply, under limited circumstances, of substances with long histories of safe use for which there exist no practicable substitutes and the precipitous prohibition of which would adversely affect consumers and the food supply; and

- agency decision-makers should be directed to subject all available data concerning a suspect substance to scientific review by qualified experts independent of the agency involved before using such data as the basis for regulatory action on a substance.

Definition of "Safe"

The term "safe" appears in a number of provisions in current law. Nowhere, however, is that term defined. As a matter of legislative history and judicial interpretation, the term has come to mean "a reasonable certainty of no harm." As applied, this is a "zero risk" standard of safety. Our increasing ability to identify the presence of potentially harmful substances in food in infinitesimally small amounts that do not present significant risks to humans makes it clear that continued pursuit of absolute safety is impractical and undesirable. If we are to continue to enjoy an abundant, healthful and economical food supply, we must distinguish between identified risks to human health and those that are insignificant.

When he was Secretary of Health and Human Services, Richard S. Schweiker reached this same conclusion. Assailing the impracticality of current law, the former Secretary stated that:

> We have to recognize that the public neither wants nor expects the government to guarantee "zero risk." We have to recognize that absolute, one hundred percent safety is impossible in food as well as every aspect of a consumer society.

Inclusion in the law of a definition of "safe" that focuses upon the extent to which a substance presents risks to human health, therefore, would be one of the most important changes that could be made in the law. Regulatory decision-makers would, for the first time, have a Congressional mandate to focus their attention and resources using quantitative risk assessment techniques and other valid scientific approaches on those risks to human health which warrant regulatory intervention. They would be required to assess the nature and extent of the health risks from the probable consumption of a substance and to direct their regulatory resources to those substances that present real potential for harm.

Application of Delaney Clause

This awareness that a "zero-risk" safety standard is neither attainable nor from a practical standpoint, desirable must guide our application of the Delaney Clause as well. Under current law, that provision requires that any substance shown to cause cancer in man or animals, no matter how remote the potential for harm to humans under the substance's intended use, be banned. Certainly, the Delaney Clause is an important public health protective device that should not be repealed. However, it was much more viable scientifically when first adopted in 1958, at a time when scientists were unable either to detect the presence of chemicals in foods in parts per trillion or to assess with any degree of confidence the significance to humans of risks from a substance shown by animal studies to cause cancer.

FDA Commissioner Arthur Hull Hayes has made this point quite effectively. He has assessed the viability of the nation's food safety laws as follows:

> Although these laws have seemed to serve our nation well, they were drafted for earlier

> times. Technology now plays an even greater role in producing, packaging and distributing the various components of the food supply. In addition, science has advanced to such an extent that we are today aware of numerous low-level risks especially from carcinogens that were previously unrecognized.

In short, the Delaney Clause should no longer be applied to substances that present insignificant risks to human health under their intended conditions of use.

Consideration of Benefits

Current law also is shortsighted in prohibiting the agencies from taking into consideration in making food safety regulatory decisions the benefits to human health that a substance might offer. Yet, there are many substances that perform extremely important functions in food in terms of preservation, nutritional value, and dietary management, for example. Such benefits can no longer be ignored when an agency is considering prohibiting the use of a substance.

We do not suggest that an agency simply weigh the risks and benefits presented by a substance before prohibiting its use as if those factors somehow could be measured objectively on a scale. Nor should benefits even be considered in all cases. On the other hand, a substance that has been safely used in food for a long period of time and for which there exists no practicable substitute should not be sacrificed, if it provides major benefits to consumers that make its risks acceptable.

Phase-Out Authority

It also is important that the law be amended to authorize USDA and FDA to provide for the gradual elimination from the food supply of substances that are no longer considered "safe." This authority is especially critical for substances that have been used safely for a long period of time and for which there exists no practicable substitute. As was clearly demonstrated by the nitrite experience, such specific phase-out authority represents one of the most pressing pragmatic needs in the area of food safety law reform, if massive disruptions in the nation's food supply are to be avoided.

It is estimated that more than nine billion pounds of cured meat products are produced in the United States each year. Much of this is processed with sodium nitrite. There is no known adequate substitute for nitrite as a botulism preventative. Had nitrite been banned, a major disruption of the national meat supply would have resulted, with bacon, ham and sausage as we know them today becoming scarce.

Peer Review of Scientific Data

The changes we have suggested so far are based upon the indisputable premise that agencies must be permitted -- indeed, obligated -- to apply the best technology and most sophisticated science in making food safety regulatory decisions. The agencies' discretion, however, must not go unchecked. The only way to ensure that agencies bring the best scientific expertise to bear before taking any regulatory action when a serious question about the safety of a food substance arises is to direct them to establish Advisory Committees to review data and make recommendations upon which the agencies would rely.

As noted earlier, not until Congressional pressure was brought to bear on FDA and USDA was outside scientific peer review undertaken of the study results upon which that agency was prepared to ban nitrite. This was notwithstanding the more than 25 studies on the safety of nitrite that were in existence at that time. Yet, the agencies felt compelled to act because current law does not mandate independent evaluation of the data in question. In fact, the law effectively discourages agencies from exercising their judgment in this regard. This is why Congressman Thomas Foley, Chairman of the House Agriculture Committee during the nitrite crisis, concluded that:

> Because of the automatic and categorical operation of some of our food safety laws, a Commissioner of FDA or a Secretary of the Department of Agriculture might be forced to take action that they think is wrong not necessarily to protect the public health, which, in fact, could be dangerous to the public health.

The nitrite experience exemplified the type of unnecessary public scare that might have been ameliorated or even avoided completely had external peer review been employed. Several such incidents in the past two decades have triggered serious false alarms accompanied by public confusion, economic harm to the food industry, and a loss of faith in government food safety decisions. Peer review by scientists independent of the agencies making food safety decisions should help ensure that correct scientific review procedures are followed and that government, industry and consumers are all confident in the food safety decisions that are made.

As Secretary of Agriculture John Block has stated:

> Biased and uninformed decisions by government agencies must be prevented in the future. Regulatory decisions must be reviewed by an independent panel of scientific experts and explored thoroughly to prevent such misjudgments from ever happening again.

Conclusion

Our recommendations for modification of the food safety laws represent but a few of the changes that experience has convinced us are needed. We hope that the issues that we have addressed and those that others will certainly identify will help focus this Committee's review of the nation's food safety laws in a comprehensive and constructive fashion.

As we pointed out at the beginning of this statement, the problem under scrutiny by this Committee does not concern the fundamental safety of the food supply. America is fortunate to have the safest and most wholesome food supply in the world. The problem concerns the laws under which that food supply is regulated. These laws prevent regulators from taking advantage of modern day technology. They are laws that prohibit regulators from exercising good scientific judgment in making food safety decisions. They are laws that the prestigious National Academy of Sciences has called "complicated, inflexible and inconsistent." They are laws that former Health and Human Services Secretary Joseph A. Califano has said are "knee-jerk" in their operation and which "should be changed."

This Committee must be concerned that the laws under which food is regulated ensure that consumers receive only safe food. The Committee must also be concerned that consumers have faith in decisions made by government agencies and that they are not be deprived of beneficial food substances because of laws that do not allow regulators to think.

Now is the time for Congress to review these laws and consider revising them -- at a time when it does not face a food safety "crisis." Congress is well equipped to improve upon laws that do not work well. Certainly, this is preferable to preventing the federal agencies from enforcing an outdated law, something that Congress has had to do on a number of occasions in recent years.

We greatly appreciate this opportunity to present our views, and will be pleased to work with the Committee as it further considers this issue and begins focusing upon the precise legislative language that might be considered to implement whatever changes in the laws are determined to be appropriate at this time.

* * * *

The CHAIRMAN. We will now turn to Mr. Ebert, who represents the National Food Processors Association, as vice president for research.

Mr. Ebert?

STATEMENT OF ANDREW G. EBERT, VICE PRESIDENT, RESEARCH, DEVELOPMENT AND QUALITY ASSURANCE, PET INC., ST. LOUIS, MO., REPRESENTING THE NATIONAL FOOD PROCESSORS ASSOCIATION

Mr. EBERT. Thank you, Mr. Chairman.

My name is Andrew Ebert. I am vice president for research, development, and quality assurance with Pet, Inc., in St. Louis. Today I am representing the National Food Processors Association.

I would also like to introduce you to the associations counsel, H. Edward Dunkelberger, Jr., of Covington and Burling here in Washington, and also acknowledge his help in drafting our detailed statement, which has been submitted for the record.

I also speak with much empathy for a number of the other pharmacologists and toxicologists who have been here. My doctorate is in that area. I have worked with food safety evaluation for about 15 years, and I am well aware that a mouse is not a small man.

NFPA is a scientifically and technically based trade association representing about 600 member companies. Food safety has been the primary mission of our laboratories since 1913. Our mission continues to this day with laboratories in Berkeley, Calif., Seattle, Wash., and a new state-of-the-art and science laboratory facility scheduled to open this year here in Washington, the lab is, of course, our pride and joy.

While food safety is important, we must consider the fact that many in our society, by their very lifestyles expose themselves to far greater risks than those posed by our food supply. Congress, the regulatory agencies, and the regulated industries recognize that food is a mixture of complex chemicals and that with our current state of knowledge it is virtually impossible to know how all food components will react with man, especially in those persons suffering a variety of diseases and health problems. To think that extensive congressional action, regulatory control, or product formulation can totally protect all persons ignores the toxicological facts of life.

Safety is just one of several attributes we want in our food supply. Others include availability, affordability, preference, taste, enjoyment, even recognition of ethnic and geographical backgrounds. A safe food supply that is beyond the reach of some for economic reasons or insufficient at certain times is of little consequence to those for whom the supply falls short.

The chairman has asked us to address the issue of how recent scientific and technological developments have affected food safety regulation. We believe there are at least two quite different ways in which science makes it necessary to reassess our food safety laws. The issue of improved toxicological testing and analytical techniques have been addressed in detail by other witnesses—indeed, by you, Mr. Chairman. The second, new technology, is of great interest to us at NFPA, since it has and will cause rapid changes in our industry. There are numerous new package forms available to the consumer ranging from rigid containers, non-rigid packages, pouches, envelopes et cetera, all designed to deliver safe, nutritious, convenient, and economical food.

Taken together, the developments in the improvement of analytical techniques and toxicological testing cast into doubt the legal status of many customary foods, even though the risk is insignificant or purely hypothetical. The absolute strictures of the Delaney clause have been interprested as leaving no room for judgment or scientific evaluation. There is no question in our mind that a zero risk concept, rigorously pursued, will eventually threaten the availability, wholesomeness, and acceptability of food products currently recognized as important parts of the food supply.

The changes in our food supply being brought about by science and technology must, of course, meet the requirements for safety and wholesomeness. It is equally important, however, that changes which are perceived as otherwise desirable not be prohibited or unduly delayed because of an unscientific adherence to a zero risk safety standard.

Although a zero-risk standard may have been tolerable for a stable food industry, it becomes increasingly costly and burdensome at a time when many factors are militating in favor of change, or at least the process of change, that permits the introduction of new foods, new processes, and new packages, as we see in our industry.

The chairman has also requested that we address ways in which the law should be revised in order to accommodate advances in science and technology. We believe that the structure and content of the Federal Food, Drug, and Cosmetic Act reflects and gives effect to sound policy judgments with respect to the safety of the food supply. As articulated by Dr. Roberts, we endorse maintenance of the act in its present form and substance, with just a few modifications.

NFPA believes that the Delaney clause and the general safety clauses of the act should be amended to make explicit the applicability of the concept of significant risk. In our view the time has come for Congress to provide the Food and Drug Administration the discretion required for implementation of the Delaney clause to allow for the exercise of scientific judgment where the toxicological data and risk assessment support a conclusion that there is no significant risk to humans from the use of a particular substance.

On the matter of consideration of benefits in food safety decisionmaking, this association is strongly of the view that except under very limited circumstances, safety considerations alone should apply in determining whether a particular substance should be permitted or tolerated in a food. For the most part, benefit considerations are and should remain irrelevant in the administration of the act. Under the current act, the benefit, value, or cost of a substance are not taken into account in determining whether an additive should be approved or the presence of a substance in a food should be tolerated. We agree with those who contend that the question of value or benefit of a new additive should be left to the producers, processors, and consumers of food.

In our written testimony we also discuss section 406 of the act, which prescribes the limited circumstances under which FDA may take into account the need for an adequate food supply. This section directs FDA to prescribe tolerances for added poisonous or deleterious substances which cannot be avoided in food even when produced under good manufacturing practices.

Section 406, was enacted as part of the 1938 act in order to provide that substantial quantities of food would not be eliminated from the food supply because they contained an unavoidable environmental contaminant or amounts of a substance that was required in the production of the food. In recent years FDA has acted under section 406 to preclude a total ban of important foods containing low levels of such unavoidable materials as we heard today—alfatoxin, mercury, and PCB's.

Thus, FDA has in administering this provision given weight to the need to avoid disruption in the food supply and to assure availability of nutritious, economical foods. Fundamental to the issuance of a tolerance or action level in each case was the determination that the substance was unavoidable by good manufacturing practice or required in the production of food.

FDA has further interpreted section 406 as not being applicable to food additives which are subject to regulation under section 409. We propose that section 406 be amended to authorize the application of that provision to food additives, as well as to prior sanctioned substances and environmental contaminants, if they are unavoidable by good manufacturing practice, are required in the production of food, or have no practicable substitute and a substantial history of use.

In summary, NFPA believes that the present food safety laws are sound. It is our position that the Food, Drug and Cosmetic Act should, not be dismantled, but modified to reflect current science.

NFPA is satisfied that FDA has sufficient legal authority to assure the safety of the food supply insofar as governmental regulatory authority can contribute to the achievement of that result. Food safety is necessarily the collective goal of FDA, USDA, State and local health agencies, and the producers, processors, and distributors of foods as well. NFPA and its members continue to pledge our support in maintaining the safety of the food supply.

Thank you.

[The prepared statement of Mr. Ebert and responses to questions asked follow:]

Summary
Statement of the
National Food Processors Association
Before the
Committee on Labor and Human Resources
U.S. Senate
On Federal Food Safety Laws
June 10, 1983

Mr. Chairman:

My name is Andrew G. Ebert and I'm representing the National Food Processors Association. Accompanying me is the Association's counsel, H. Edward Dunkelberger, Jr. of Covington & Burling here in Washington. NFPA is a scientifically and technically based trade association representing about 600 member companies. Food safety has been the primary mission of our laboratories since 1913. Our mission continues to this day, with laboratories in Berkeley, California, Seattle, Washington, and a new state-of-the-art and science facility scheduled to open this year here in our nation's capital.

Our views on scientific and public policy issues relating to food safety laws are described in detail in our written statement filed with the Committee. I shall present a brief summary.

While food safety is important, we must consider the fact that many in our society, by their very lifestyles, expose themselves to far greater risks than those posed by our food supply. Congress, the regulatory agencies, and the regulated industries recognize that food is a mixture of complex chemicals and that with our current state of knowledge it is virtually impossible to know how all food components will react with man, especially in those persons suffering a variety of diseases, and health problems. To think that extensive Congressional action, regulatory control or product formulation can totally protect all persons ignores the toxicological facts of life.

Safety is just one of several attributes we want in our food supply. Others include availability, affordability, preference, taste, enjoyment, even recognition of ethnic and geographical backgrounds. A safe food supply that is beyond the reach of some, or insufficient at certain times, is of little consequence to those for whom the supply falls short.

The Chairman has asked us to address the issue of how recent scientific and technological developments have affected food safety regulation. We believe there are at least two quite different ways in which science makes it necessary to reassess our food safety laws. The issue of improved toxicological testing and analytical techniques have been addressed in detail by other witnesses. The second, new technology, is of great interest to NFPA, since it has and will cause rapid changes in our industry. There are numerous new package forms available to the consumer, ranging from rigid containers, non-rigid packages, pouches, envelopes, etc., all designed to deliver safe, nutritious, convenient and economical food.

Taken together, the developments in the improvement of analytical techniques and toxicological testing cast into doubt the legal status of many customary foods, even though the risk is insignificant or purely hypothetical. The absolute strictures of the Delaney Clause have been interpreted as leaving no room for judgment or scientific evaluation. There is no question that a zero risk concept, rigorously pursued, will eventually threaten the availability, wholesomeness and acceptability of food products currently recognized as important parts of the food supply.

The changes in our food supply being brought about by science and technology must, of course, meet requirements for safety and wholesomeness. It is equally important, however, that changes which are perceived as otherwise desirable not be prohibited or unduly delayed because of an unscientific adherence to a zero risk safety standard.

Although a zero risk standard may have been tolerable for a stable food industry, it becomes increasingly costly and burdensome at a time when many factors are militating in favor of change, or at least a process of change that permits the introduction of new foods, new processes and new packages.

The Chairman has also requested that we address ways in which the law should be revised in order to accommodate advances in science and technology. We believe that the structure and content of the Federal Food, Drug and Cosmetic Act reflects and gives effect to sound policy judgments with respect to the safety of the food supply. We endorse maintenance of the Act in its present form and substance, with just a few modifications.

NFPA believes that the Delaney Clause and the general safety clauses of the Act should be amended to make explicit the applicability of the concept of significant risk. In our view the time has come for Congress to provide the agency the discretion required for implementation of the Delaney Clause to allow for the exercise of scientific judgment where the toxicological data and risk assessment support a conclusion that there is no significant risk to humans from the use of a particular substance.

On the matter of consideration of benefits in food safety decision-making, this Association is strongly of the view that except under very limited circumstances, safety considerations alone should apply in determining whether a particular substance should be permitted or tolerated in a food. For the most part benefit considerations are and should remain irrelevant in the administration of the Act. Under the current act, the benefit, value or cost of a substance are not taken into account in determining whether an additive should be approved or the presence of a substance in a food should be tolerated. We agree with those who contend that the question of value or benefit of a new additive should be left to the producers, processors and consumers of foods.

Our written testimony also discusses Section 406 of the Act, which prescribes the limited circumstances under which FDA may take into account the need for an adequate food supply. This section directs FDA to prescribe tolerances for "added" poisonous or deleterious substances which cannot be avoided in food even when produced under good manufacturing practices.

Section 406 was enacted as part of the 1938 Act in order to provide that substantial quantities of food would not be eliminated from the food supply because they contained an unavoidable environmental contaminant or amounts of a substance that was required in the production of the food. In recent years FDA has acted under Section 406 to preclude a total ban of important foods containing low levels of such unavoidable contaminants as aflatoxin, mercury and PCBs.

Thus, FDA has in administering this provision given weight to the need to avoid disruption in the food supply and to assure availability of nutritious, economical foods. Fundamental to the issuance of a tolerance or action level in each case was the determination that the substance was unavoidable by good manufacturing practice or required in the production of food.

FDA has interpreted Section 406 as not being applicable to food additives which are subject to regulation under Section 409. We propose that Section 406 be amended to authorize the application of that provision to food additives, as well as to prior sanctioned substances and environmental contaminants, if they are unavoidable by good manufacturing practice, are required in the production of food, or have no practicable substitute and a substantial history of use.

In summary, NFPA believes that the present food safety laws are sound. It is our position that the Food, Drug and Cosmetic Act should not be dismantled, but modified to reflect current science.

NFPA is satisfied that FDA has sufficient legal authority to assure the safety of the food supply, insofar as governmental regulatory authority can contribute to the achievement of that result. Food safety is necessarily the collective goal of FDA, USDA, state and local health agencies, and the producers, processors and distributors of foods. NFPA and its members continue to pledge our support in maintaining the safety of the food supply.

RESPONSE TO SENATOR HATCH'S QUESTION

Effect of Current Law on Innovation

In our judgment, current law does stifle innovation, particularly in the development of new types of packaging for processed foods. As an example, the development of rigid plastic containers for foods has had a number of advantages for consumers. FDA's initially strict interpretation of the Delaney Clause regarding acrylonitrile and polyvinyl chloride (PVC), however, substantially inhibited the full range of development of these containers during the past decade.

Both acrylonitrile and PVC can be used to make rigid containers that provide a wide variety of food products. Such containers are substantially lighter than the equivalent size containers made of other rigid materials, thus providing easier handling and savings to the consumer in lower freight costs. In addition, such containers do not shatter on impact, eliminating a potential safety hazard associated with some other existing containers.

The starting material for both acrylonitrile and PVC are chemical monomers that have been found to be carcinogenic. The manufacturing process for the finished polymer inevitably leaves trace amounts of residual monomer than can migrate from the container wall into either the atmosphere or the food in the container. FDA's initial approach was to project the theoretical migration levels, characterize the migratory monomer as part of the container, and as a result, conclude that the container material could not be approved or would have to be withdrawn from the market because it introduced a carcinogenic substance into the food supply contrary to the Delaney Clause.

FDA has recently proposed to redefine its approach, so that only the finished container material as a whole would be subject to the Delaney Clause (neither acrylonitrile polymer nor PVC is carcinogenic) and the residual monomer would be treated as a "constituent" that would not render the product unsafe if it posed a "negligible" risk of cancer (generally defined as a risk of less than one cancer in a million lifetimes).

This "constituents policy" has been criticized in administrative proceedings, and is presently under challenge in judicial review of a color additive approval. FDA's authority so to define "constituents" out from under the Delaney Clause is thus not certain.

There is another more subtle effect of current law on innovation. Food industry research and development executives have a strong sense that absolute strictures of the Delaney Clause foster inflexibility in our food regulatory structure quite aside from considerations of safety. These executives are conscious of the latent threat that a minute trace of some residue can wipe out years of dedicated work and millions of dollars of research and can render expensive equipment obsolete. That awareness has to infect their thinking and affect their initiative in planning and executing research and development of new food products, packages, and processes. Likewise, the Delaney Clause's absolutism inevitably has to influence FDA's thinking and judgment.

This may help to explain why one of the most exciting developments in food preservation today, known as aseptic processing, is just now coming onstream in the United States. This processing technology has been widely used in Europe for more than a decade. Yet it was only in Janaury 1981 that FDA approved the use of hydrogen peroxide to sterilize certain kinds of containers for use in aseptic systems.

The mindset fostered by the rigidity of the Delaney Clause may also account for the fact that it is only now that government regulations are being proposed that would give FDA a rationale for permitting the use of radiation to sterilize foods. This follows more than three decades of extensive research and development work in which the technology to satisfactorily preserve a wide variety of foods by ionizing radiation has been worked out and the appropriate toxicology and evaluation studies have been completed.

RESPONSE TO SENATOR GRASSLEY'S QUESTIONS

Definition of Safe

Senator Grassley has called attention to the fact that in the discussion of the definition of "safe" in the Cabinet Council on Human Resources Working Group's final recommendations on food safety reform, the following statement is made: "Some segments of the industry will say that the Working Group's definition still will be interpreted as a zero risk standard. However, other segments of industry will find the definition acceptable." Senator Grassley asked that NFPA indicate which segment of the industry it is in with respect to the Working Group's recommended definition of safe.

In its comments to the Subcabinet Council Working Group on Food Safety, NFPA objected to their approach to the definition of "safe" on the ground that it would create unnecessary and avoidable ambiguity and controversy. The basis for this position was set forth in NFPA's written comments to the Subcabinet Council Working Group, as follows:

> "NFPA Proposal. NFPA is in full agreement with the Working Group that both the limitations of modern science and the necessity of maintaining an adequate and acceptable food supply militate against the application of an absolute standard of safety in the Act. But in our view the definition of safe in the Working Group's Second Draft does not adequately achieve the intended purpose.

"Discussion. The issue papers do not make clear why the Working Group has chosen to define safety in terms of a negligible risk in the Second Draft, as compared to the insignificant risk language of the first draft. Absent an authoritative explanation of the difference in meaning between the two terms, we see no reason why 'negligible risk' should be used in place of 'insignificant risk.' There are two other aspects of the definition of 'safe' in the Second Draft which give us some concern.

First, the Working Group has inexplicably sought to employ a two-stage definition by first defining 'safe' in terms of a reasonable certainty of 'no harm' and then explaining that the term 'no harm' may be demonstrated by a showing that the risks of harm are 'negligible.' This approach is in direct conflict with a basic principle of statutory drafting that counsels strongly in favor of using and defining words in a manner generally consistent with their commonsense meaning. The first sentence of the definition plainly implies a zero risk philosophy, whereas the clarifying sentence suggests something entirely different.

"This difficulty with the definition of 'safe' in proposed Section 201(u) is significantly aggravated under the Working Group's proposed addition to Section 409(c)(3), which precludes application of the Delaney Clause if it is demonstrated that there is a reasonable certainty that 'no harm' to humans will result from the use of a substance. We assume that in interpreting this 'no harm' language the second sentence in proposed Section 201(u) is intended to make the negligible risk concept applicable. The obvious difficulty with this drafting approach is that the sentence clarifying the meaning of 'no harm' is found in the definition of 'safe,' which term is not found in the proposed Delaney proviso.

"At best, the Working Group's drafting approach is clumsy and confusing. Upon first encountering the proposed added Delaney proviso readers might reasonably conclude that 'no harm'

> embodies a zero risk standard, unless they happened upon the definition of the term 'safe' in the definitional sections of the Act, and decided that the second sentence of that definition was intended to apply not only to the term 'no harm' as used in the definition of 'safe,' but also to 'no harm' where it is used elsewhere. At worst, the Working Group's approach may defeat the purpose of eliminating the zero risk concept from the Delaney Clause. Accordingly, we urge that the Working Group return to the one-stage, insignificant risk wording, and that the proposed added proviso to the Delaney Clause be rephrased so as to make explicitly clear that the insignificant risk concept applies to the Delaney Clause.
>
> "Our second objection to the Working Group's Second Draft is that it purports to clarify the concept of safety only in Sections 408, 409, 512, and 706. The term 'safe' is also found in Section 201(s) (within the GRAS clause food additive exclusion), and in Section 406. In addition, it must be made clear that the elaboration of the term safe has equal application to the term 'injurious to health' as it is used in Section 402. Although there is some wording in the Working Group's issue papers that might be read to the contrary, we cannot believe that it is seriously intended that the concept of 'safe' in Section 409 be interpreted in terms of insignificant risk, but that absolute safety be required under Section 402(a). Nevertheless, that might well be the effect of the Working Group's draft approach. We urge that this proposal be revised so as to make clear that the insignificant risk concept also applies under Section 402 in determining whether a food is injurious to health."

In summary, the Working Group's proposed two-step approach to defining "safe" is more likely to create confusion and controversy than to provide the necessary relief from the straitjacket of existing statutory provisions and interpretations.

Benefits to be Considered In Risk-Benefit Analysis

Senator Grassley has also asked what benefits should be considered in determining the lawfulness of food and food ingredients.

NFPA's position with respect to the consideration of benefits in the context of food safety is that FDA should be authorized to take benefits into account for food additives to the same extent that it has done so in its implementation of Section 406 for environmental contaminants and prior sanctioned substances. Our basis for this position is set forth at some length in the enclosed memorandum of March 3, 1983. The memorandum reviews several relatively recent proceedings in which FDA has applied Section 406 in establishing tolerances for certain unavoidable environmental contaminants or required or unavoidable prior sanctioned substances. In each of these proceedings FDA determined that a total ban would have resulted in a substantial disruption of the food supply and elimination from the market of economical, wholesome and nutritious foods.

NFPA is satisfied that these Section 406 precedents provide an appropriate basis for FDA determinations with respect to food additives. The reasons for this conclusion may be summarized as follows:

(1) Formal food additive determinations under Section 409 should be confined solely to questions of safety, in order to assure that benefit considerations will not become involved in submissions or decisions relating to food additives under Section 409.

(2) The standards that are now applied in Section 406 in promulgating tolerances for unavoidable contaminants or required or prior sanctioned substances may appropriately be applied to food additives, with the result that benefit considerations will be focused only in that section of the Act, and under the same general standards and procedures.

(3) The use of Section 406 in this fashion will make available a series of precedents for guidance in future determinations. An attempt to formulate new benefit standards in Section 409 or elsewhere in the Act would necessarily result in greater uncertainty and controversy.

March 3, 1983

MEMORANDUM

Re: Proposed Use of Section 406 For the Regulation Of Required or Unavoidable Food Additives With A Long History of Use and No Practicable Substitute

A number of recent proposals for amendment of the food safety provisions of the Federal Food, Drug and Cosmetic Act would incorporate into section 409 a requirement that FDA give consideration to the benefits of additives which have a long history of use and no adequate substitute. For example, the September 13, 1982, draft language prepared by the Subcabinet Council Working Group on Food Safety provides that in determining whether to issue or repeal a food additive regulation for an additive that has a substantial history of use in food and for which there is no practicable substitute, the FDA shall base its determination on whether a fair evaluation of the evidence "demonstrates that the risks to human health presented by such use of such food additive are acceptable on account of the benefits to human health from such use of such food additive."*/

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*/ The draft statutory language does not define "health benefits," but the accompanying issue paper suggests "that the scope of health benefits be broad enough to include consideration of factors such as a substance's use for nutritional purposes or dietary mangagement and the substance's role in providing an adequate food supply." It suggests further that the scope of benefits should not include "nonhealth benefits such as cost of food" or "desire of consumers."

The National Food Processors Association and some others have urged reconsideration of this approach, and have proposed instead that the issues to which the risk-benefit provisions of the Working Group's Second Draft are directed should be dealt with by appropriate amendment to section 406. The basis for this proposal is summarized in NFPA's comments of December 10, 1982, on the Working Group's Second Draft, as follows:

> "The proposed risk-benefit assessment provisions in the Second Draft are a substantial improvement over those contained in the first draft. We are satisfied, however, that any possible benefit considerations for a questioned substance in long use and for which there is no substitute should be dealt with under section 406 rather than by an amended section 409. It makes far more sense, we believe, for section 409 to deal solely with issues of safety so that there will be no possibility that benefit considerations might find their way into routine food additive submissions or decisions.
>
> "Our suggested modification of section 406 would authorize the application of that provision to food additives, as well as to prior sanctioned substances and environmental contaminants, if they are unavoidable by good manufacturing practice, are required in the production of food, or have no practicable substitute and a substantial history of use. Although there have been few formal actions under section 406, the agency has been developing a consistent interpretation of that provision on a case-by-case basis, spelling out the extent to which it is necessary and appropriate to take into account factors other than safety. It

> makes good sense to take advantage of that experience and to assure continuity in the standards and factors to be considered in establishing tolerances for substances which are required, unavoidable, or for which there is no substitute. The Working Group's proposal, on the other hand, would write new risk-benefit considerations into section 409 and would involve the use of new statutory concepts, standards, and procedures.
>
> "We submit that section 406, slightly modified as we propose to make it applicable to food additives, would be ideally suited to deal with the occasional case when safety questions are raised with respect to a required, unavoidable, or unique substance with a substantial history of use.. A substance not meeting one of these narrow criteria would be dealt with under the basic adulteration or food additive provisions of the Act, which would continue to deal with questions of safety."

Some have questioned this proposed use of section 406 on the ground that that section does not appear explicitly to require that tolerances be promulgated only for additives for which there has been a demonstration of need. They contend that long history of use and the absence of a practicable substitute should not alone justify the continued use of a questioned substance, and that there should be a further requirement of a finding that the substance provides benefits commensurate with whatever risks may be involved in its use.

The fact is, however, that section 406 has been interpreted and applied by FDA to provide for just such a consideration of need for food unavoidably containing an environmental contaminant or for the required or unavoidable use of a prior sanctioned substance. As the NFPA statement quoted above points out with respect to section 406, "the agency has been developing a consistent interpretation of that provision on a case-by-case basis, spelling out the extent to which it is necessary and appropriate to take into account factors other than safety." This memorandum will review the application of section 406 in recent years to environmental contaminants and prior sanctioned substances, with particular emphasis on the criteria which the agency has considered in reaching determinations under that section. In our view, this experience in the implementation of section 406 makes that section far more appropriate for the regulation of unavoidable, required, or unique food additives with a long history of use than the various proposed revisions to section 409 which would employ totally new statutory and regulatory concepts.

Current FDA Procedures for Regulating Added Poisonous or Deleterious Substances in Food

FDA proposed in 1974, and adopted in 1977, regulations to implement sections 402(a) and 406 of the Act establishing procedures for regulating poisonous or deleterious substances in foods.[*/] The preamble to the proposed and final regulations set forth at some length FDA's interpretation of sections 402(a) and 406 and their application to unavoidable but added poisonous or deleterious substances in food. Section 406 was described in the preamble to the proposed regulation as follows:

> "When a tolerance is established under the provisions of section 406, the act requires it to be set at the level necessary for the protection of the public health taking into account the extent to which the substance cannot be avoided and the other ways in which the consumer may be affected by the same or other poisonous or deleterious substances." 39 Fed. Reg. 42745.

It was further explained in the preamble that the agency would adopt action levels rather than formal tolerances when circumstances warranted, and that "such action levels are similar to a formal tolerance in basis and effect" since the agency "takes into account the question of its unavoidability, a policy embodied in section 406 of the act."[**/] "Thus," the agency explained, "an action level is based on the same criteria as a tolerance, except that an action level is temporary until the appearance of more stable circumstances makes a formal tolerance appropriate."[***/]

[*/] 21 C.F.R. Part 109; proposed at 39 Fed. Reg. 42743 (Dec. 6, 1974), and finally adopted at 42 Fed. Reg. 52814 (Sept. 30, 1977).

[**/] 39 Fed. Reg. 42745.

[***/] *Ibid*.

The regulations proposed and ultimately adopted set forth the criteria for promulgating tolerances or action levels for unavoidable contaminants as follows:

> "A tolerance for an added poisonous or deleterious substance in any food may be established when the following criteria are met:
>
> "(1) The substance cannot be avoided by good manufacturing practice.
>
> "(2) The tolerance [or action level] established is sufficient for the protection of the public health, taking into account the extent to which the presence of the substance cannot be avoided and the other ways in which the consumer may be affected by the same or related poisonous or deleterious substances." 21 C.F.R. § 109.6(b)(1) and (2).

The general regulations thus do little more than restate the statutory language in describing the criteria that will be considered by the agency in promulgating section 406 tolerances or action levels. The agency's interpretation of this language is made clear, however, in its proposed and final actions with respect to particular substances under this general authority. As stated by former FDA Chief Counsel Richard Merrill, "the agency has interpreted section 406 as permitting consideration of the food's value, as well as the contaminant's toxicity and the extent to which its occurrence can be controlled."*/

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*/ Merrill, Regulating Carcinogens in Food: A Legislator's Guide to the Food Safety Provisions of the Federal Food, Drug and Cosmetic Act, 77 Mich. L. Rev. 171, 200 (1978).

Actions Levels and Tolerances For Specific Environmental Contaminants

In December of 1974, in the same issue of the Federal Register in which the general regulations were proposed for the regulation of poisonous or deleterious substances in food, FDA published notices of proposed rulemaking for the promulgation of tolerances or action levels for several substances. One of the substances addressed was aflatoxin in shelled peanuts and peanut products used as human foods.[*/] In the preamble to the proposed tolerances for aflatoxins FDA explained the nature and source of aflatoxins in peanuts, and concluded that "the complete prevention of mold growth and aflatoxin production in peanuts appears unattainable at the present time." Having thus determined that aflatoxins were unavoidable in peanuts, the agency then addressed the factors to be considered in establishing a tolerance under section 406:

> "Thus, in determining an acceptable level for aflatoxins in shelled peanuts and other peanut products, the Commissioner considered all of the available information and sought to bring into balance four factors:
>
> "1. The need to minimize human exposure to aflatoxins;
>
> "2. The capabilities of sampling procedures and analytical methods to detect, measure and confirm the aflatoxins;

[*/] 39 Fed. Reg. 42748-52.

> "3. The capability of agricultural and manufacturing technology to prevent and remove contaminated peanuts; and
>
> "4. The *need for the continued availability of a low cost protein source (i.e.,* peanuts) . . . ." 39 Fed. Reg. 42750 (emphasis added).

The agency thus made clear its interpretation that under section 406 it is called upon to take into account, among other things, the need for and value of the food in which the contaminating substance is found. This interpretation of section 406 is fully consistent with the legislative purpose of Congress in enacting that section. As explained by Richard Merrill, Congress included section 402(a)(2)(A) and section 406 in the 1938 Act:

> "to permit the FDA to establish tolerances for added poisonous or deleterious substances that provide some benefit -- either because they cannot be avoided in some foods that are considered important or because their use contributes significantly to food production."*/

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*/ Merrill, *supra*, at 195. On the basis of his review of the legislative history of section 406, Merrill concludes that one class of substances Congress had in mind in enacting section 406 was pesticides, which were "regarded as absolutely *essential in the production of our supply of fruits and vegetables*." The then Commissioner of FDA emphasized in his testimony, however, that the authority to establish tolerances was by no means limited to pesticide residues. *Id*. at 197 n.90 (emphasis added).

In applying this interpretation to aflatoxin in peanuts, the agency discussed in the preamble to the proposal the consequences and feasibility of setting the tolerances at various specified levels. The agency considered reducing the then current informal action level of 20 ppb to a level of 5 or 10 ppb, but on the basis of the data and information before it, FDA concluded that "a move to 5 ppb or 10 ppb could result in significant losses to producers, manufacturers, and consumers alike."[*/] It went on to state that "these increased losses of food would result in much _higher prices_ . . . or in _unavailability of what is generally considered a highly nutritious and useful food_."[**/] Further, the agency stated that "because there is no direct evidence that aflatoxins cause cancer in man" it "cannot conclude that there is any technological gain from lowering the permissible level to either 10 or 5 ppb."[***/] In short, "such uncertain benefit to the public health must be weighed against the clear loss of food that would result."[****/] The agency then concluded "that existing agricultural and industrial technology can combine to yield finished peanut products at or

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[*/] 39 Fed. Reg. 42750.

[**/] _Ibid_ (emphasis added).

[***/] _Ibid_.

[****/] _Ibid_.

below a 15 ppb level without causing significantly increased losses of food."[*/]

A similar analysis was undertaken by the agency in its consideration of an action level for mercury in fish and shellfish.[**/] As the basis for its action in proposing an action level under section 406, the agency stated that "mercury contamination of fish and shellfish is unavoidable," and that "control of mercury intake by consumers of fish and shellfish can be achieved only through regulation of the mercury content of the products sold."[***/] As in the case of aflatoxin in peanuts, the preamble to the proposal reviewed effects that various action levels for mercury would have on the supply of fish and shellfish. It pointed out that an action level of 0.5 ppm would permit a daily consumption of 60 grams of fish and shellfish while maintaining a ten-fold margin of safety over the level of mercury intake known to be toxic. The average consumption of fish and shellfish was recognized as being considerably less than 60 grams per day, so that the vast majority of the population would be protected by a ten-fold margin of safety. The agency went on to note:

[*/] 39 Fed. Reg. 42750-51.

[**/] 39 Fed. Reg. 42738-40.

[***/] 39 Fed. Reg. 42738.

> "It is not possible, however, to provide that same high level of protection to every person without excluding a great amount of fish and shellfish from the market . . .. An action level of about 0.18 ppm would be necessary to assure a ten-fold margin of safety for those [few] individuals who consume approximately 165 grams of fish and shellfish per day." 39 Fed. Reg. 42739.

The agency concluded that "an inordinate amount of fish would be excluded from the market by such an action level."*/ The agency then explained the significance of these data in the implementation of section 406:

> "The number of fish and shellfish that would be excluded from sale at a given action level is a reflection of the degree to which the contaminant is unavoidable. In establishing an action level, the Commissioner must consider the extent to which the contaminant is unavoidable, which is the policy embodied in section 406 of the act.
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> "In balancing the unavoidability of mercury in fish and shellfish against the need for protection of the public health, the Commissioner concludes that it would be inappropriate to exclude a vast amount of fish and shellfish from the market in order to provide a large margin of safety for those who consume far more than the average person." 39 Fed. Reg. 42739.

Accordingly, the agency proposed an action level of 0.5 ppm.

Five years later FDA reconsidered the question of an appropriate action level for mercury in fish and shellfish.

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*/ 39 Fed. Reg. 42739.

On the basis of new data the agency concluded that "the values used in 1974 for estimating a tolerable level of methylmercury for humans may have been too low."*/ It accordingly determined that a 1.0 ppm action level for swordfish and freshwater fish "would provide adequate protection to consumers,"**/ and would be responsive to the issues raised by the National Marine Fisheries Service in their submission to FDA:

> "The NMFS concluded that a 1.0 ppm action level would protect consumers as much as does the 0.5 ppm level. Also, the higher level would provide a significant economic benefit to those industries most seriously affected by regulatory actions under the 0.5 ppm guideline and would enhance the future development of a number of presently underutilized fisheries. The report also stated that the less restrictive regulatory approach it recommended would significantly increase consumer confidence in seafood." 44 Fed. Reg. 3992.

Once again FDA took into account the need for an adequate supply of fish and shellfish, and the importance of maintaining a viable industry to provide these foods to consumers. Similar considerations came into play in 1977 when FDA proposed to reduce informal action levels for PCBs in several classes of foods on the basis of new toxicological data and the agency's conclusion that lower levels of PCBs could be maintained. With respect to fish, the agency indicated that it had under consideration a reduction of the action level from 5 to 1 ppm, but that "under the provisions of section 406 of the act, the Commissioner is required, in establishing a tolerance, to consider the extent to which the contaminant is unavoidable."*/ The Commissioner set out at some length an analysis of the impact of various tolerance levels on the supply of fish,**/ and reviewed the safety and

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*/ 44 Fed. Reg. 3992.

**/ *Ibid.*

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*/ 42 Fed. Reg. 17492.

**/ "The Commissioner has determined that establishment of a tolerance at 1 ppm for fish sold in interstate commerce would have a substantially adverse impact on this country's commercial freshwater fishing industry and, to a lesser extent, the commercial marketing of saltwater species. He estimates that the loss to fresh and marine fisheries as a result of enforcing this legal limit would be a maximum total landed value of $18 million or $127 million after processing (cleaning, canning, distributing, retailing, etc.). (Reference 39). The Commissioner points out that because most commercial fishing is done by fairly small operators who may specialize in one or two species, the elimination of any species, even though it may account for only a fraction of the total catch, could be disastrous for them.

"Accordingly, the Commissioner has examined the economic impact of proposing a tolerance for PCB's in fish at 2 ppm and has considered whether this level would provide an acceptable margin

(continued)

consumption data with respect to PCBs in foods, before stating his conclusion as follows:

> "Thus, the Commissioner concludes that a tolerance of 2 ppm will provide adequate protection for all but those population groups that consume above average amounts of freshwater fish from contaminated waters. Moreover, a 2 ppm tolerance would eliminate a relatively minor percentage of marine fish and less than 25 percent of freshwater fish from commercial markets. On the other hand, although a tolerance higher than 2 ppm would be more economically desirable, such a tolerance would, based on the above analysis add to the risk for the

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(footnote continued)

> of safety to the consumer. For marine or saltwater fish, lowering the current temporary tolerance to 2 ppm would result in a loss of $1 million landed value, which would increase about seven times after processing. Thus, the total losses at a 2 ppm tolerance would be about $7 million (Reference 39). For freshwater fish the loss at the 2 ppm level would be more severe: about $7 million landed value or $49 million processed value.
>
> "The Commissioner notes that the economic loss for marine fish would be about the same at the 3 ppm level, but the dollar loss for freshwater fish would be about 40 percent of that estimated for a 2 ppm tolerance. He further notes that according to the FDA economic assessment, the current temporary tolerance of 5 ppm may be resulting in an $8 million maximum total loss for freshwater fish (Reference 39). The commercial impact of a 2 ppm level would be much less than that of 1 ppm, and limits above 2 ppm would further decrease the potential commercial impact even more." 42 Fed. Reg. 17492.

> so-called average consumer and those population groups who regularly consume freshwater fish. Therefore, in keeping with the agency objective to minimize dietary exposures to PCB's, the Commissioner concludes that a 2 ppm temporary tolerance for PCB residues in fish represents a proper balance of the safety and economic criteria of section 406 of the act." 42 Fed. Reg. 17493.

In each of these matters involving the application of section 406 to unavoidable environmental contaminants in foods the FDA has taken into consideration the need to minimize human exposure to the contaminant, the extent to which it is unavoidable, and the need for an adequate and economically available food supply. In each instance the agency's ultimate conclusion was that the tolerance or action level proposed or adopted was adequate to assure protection of the public health, and would to the extent feasible avoid ruinous destruction of large volumes of wholesome, valuable food. In exercising its statutory responsibility to take into account the extent to which the presence of a contaminant cannot be avoided in the production of a particular food, the agency has interpreted and applied section 406 to carry out the Congressional purpose of establishing action levels or tolerances which provide protection of the public health and at the same time avoid undue loss or destruction of significant volumes of important foods.

Application of Section 406 To Prior Sanctioned Substances

The agency's implementation of section 406 for the most part has focused on environmental contaminants. However, in its Advance Notice of Proposed Rulemaking relating to lead in food, FDA had occasion to consider how and under what circumstances section 406 tolerances or action levels might be adopted for a substance that is not an environmental contaminant, but instead is one that is deliberately used and serves a functional purpose in the production of food.*/ In the lead Advance Notice the agency included a somewhat extended discussion of the legal issues bearing upon the status of container-derived lead in processed foods. The agency pointed out that generally the food additive provisions of section 409 would apply to direct and indirect food additives, except when the substance in question was subject to a prior sanction and thus explicitly exempt from the statutory definition of a food additive. Although such a prior sanctioned substance would not be subject to section 409, the agency did emphasize that "the prior sanctioned use is still subject to the provisions of law that apply to added poisonous or deleterious substances."**/ The agency explained that it had some basis for concluding that container-derived lead was subject to a prior sanction, and it invited further comment and data on that issue. It then set forth its interpretation of how the Act -- sections 402 and 406 in particular -- would be applied to lead if it were indeed subject to a prior sanction:

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*/ 44 Fed. Reg. 51233-42 (Aug. 31, 1979).

**/ 44 Fed. Reg. 51239.

> "Any uses of lead that are 'prior sanctioned' are subject to regulatory action by FDA under sections 402 and 406 of the FFDC Act to the extent the food contains an added poisonous or deleterious substance that may be injurious to health, or that is not in accord with a tolerance established under section 406. The presence of lead in food can be considered poisonous or deleterious on account of the risks discussed above. Tolerances can be established for added substances, which are not food additives, if the substance is required in production or cannot be avoided by good manufacturing processes. The use of lead is necessary as a solder in the production of the tin can, but the amount of lead used should not exceed what is required or what is unavoidable under good manufacturing practices. ***
>
> "The agency believes that in establishing any action levels and tolerances for lead, it should consider various factors, including the extent to which the use of lead can be avoided and minimized in the manufacturing process, the potential for disruption of the food supply, the level of risk posed, and the ubiquitous distribution of the substance. Feasible alternatives for the current uses of the lead-soldered tin can are not generally available, and the distribution of the food supply would be disrupted if its use were precipitately curtailed. ***" 44 Fed. Reg. 51240 (emphasis added).

This passage from the lead Advance Notice makes clear the appropriate application of section 406 to substances other than environmental contaminants. As the agency notes, a tolerance or action level can be promulgated under section 406 "for added substances, which are not food additives, if the substance is required in production or cannot be avoided by good manufacturing processes." This application of section 406 to deliberately used, required substances is of course fully consistent with Congress' purpose in enacting section 406 in order to authorize tolerances for substances, such as pesticides, that are used because they are required in the production of the food supply.

Proposed Limited Expansion of Section 406

This review of the agency's implementation of section 406 in the last decade establishes that section 406 is an ideal vehicle for the regulation not only of unavoidable environmental contaminants and unavoidable or required prior sanctioned substances, but also for regulation of food additives under the limited circumstances when their use is unavoidable or required in the production of food. The concept of required in the production of food should be clarified so that it explicitly includes substances with a long history of use in the United States food supply and for which there is no practicable substitute.

As the lead proceeding makes clear, section 406 tolerances are appropriate for deliberately used prior sanctioned substances which are required in food production or cannot be avoided by good manufacturing practices. But under FDA's current interpretation of the Act, unless a substance is prior sanctioned and thus exempt from food additive regulation:

> "Tolerances under section 406 of the act (and action levels) should not be established in Part 109 for intentionally added food ingredients or for components of food contact articles that serve a functional purpose in the food contact article." 42 Fed. Reg. 52817.

The proposed amendment of section 406 would modify this interpretation only to the limited extent of authorizing section 406 tolerances for intentionally used direct or indirect food additives that meet the narrow and rigorous criteria of that section. Section 406 was enacted in 1938 because Congress concluded that the Act's safety standards for most food ingredients and components are not appropriate for those "added" substances that are unavoidably present in food or are required in the production of food. The proposed amendment of section 406 would assure the consistent application of this policy to all unavoidable or required substances -- both food additives and prior sanctioned substances.

Several food safety bills introduced in the last Congress -- including those by Senator Hatch and Congressman Gore -- as well as the first and second drafts prepared by the Subcabinet Council Working Group, proposed that food additives with a substantial history of safe use and for which there is no practicable substitute should be subject to a somewhat different safety standard than that applicable to other food additives. These bills would amend section 409 by providing for a limited risk-benefit determination for such substances. The various proposals have taken somewhat different approaches in characterizing and establishing standards for the risk-benefit determination. As we stated at the outset, NFPA is persuaded that it makes far more sense to provide for the consistent regulation of unavoidable, required or unique substances in section 406 under the policies established by Congress in 1938 and applied by FDA in implementing section 406 in recent years. The reasons for our conclusion in this regard can be summarized as follows:

(1) Since enactment of the Act in 1938 and adoption of the Food Additives Amendment in 1958, section 402(a)(1) and section 409 have been governed solely by questions of safety, and consideration of the importance and value of a food may be taken into consideration only in the

implementation of section 406. This dichotomy should be preserved, so as to assure that benefit considerations will not become involved in submissions or decisions relating to food additives under section 409.

(2) It makes no sense to fragment the Act so that one set of standards applies to unavoidable, required or unique substances regulated under section 406 (environmental contaminants and prior sanctioned substances), and a different set of standards for required or unique food additives under section 409.

(3) For at least a decade FDA has implemented section 406 in such a way as to establish precedents and give guidance for future cases. There will be no such precedents or guidance in the implementation of whatever new risk-benefit standards are written into section 409 for long used, unique food additives.

(4) As a result of the proposal to apply notice and comment rulemaking to the promulgation of section 406 tolerances, the agency will be in a position to act relatively promptly and effectively in making appropriate determinations under that section for food additives and other substances. Under the Working Group's proposals the risk-benefit determinations would be subject to the formal rulemaking procedures prescribed for section 409, with the result that the

agency would be far less able to make responsible decisions on the basis of its informed discretion, without the imposition of excessive burdens, costs and delay that necessarily accompany formal rulemaking procedures.

(5) The Congressional policy embodied in section 406 and implemented by FDA in the past decade has proved to be sensible, practical and workable. The matters that have been addressed under section 406 have raised difficult, controversial issues affecting large segments of the consuming and producing public. Everyone has not always agreed with FDA's decision in each case, but it is fair to say that there is general acceptance of the policy and criteria applied under section 406.

The CHAIRMAN. Thank you, Mr. Ebert.

We will turn now to Mr. Jerome Heckman, who is general counsel for the Society of the Plastics Industry, Inc.

We look forward to taking your testimony, Mr. Heckman.

STATEMENT OF JEROME H. HECKMAN, GENERAL COUNSEL, THE SOCIETY OF THE PLASTICS INDUSTRY, INC., WASHINGTON, D.C.

Mr. HECKMAN. Senator Hatch, thank you very much.

My name is Jerome H. Heckman of the Washington law firm of Keller and Heckman. I am general counsel for the Society of Plastics Industry, the headquarters office of which is in New York City and I am presenting this statement on its behalf.

SPI represents some 1,200 member companes and is the major national trade association of the plastics industry. We are grateful for this chance to address the serious problems of packaging materials suppliers under the current provisions of the food safety laws.

Prior to the passage of the Food Additives Amendment of 1958, the packaging industry had a generally satisfactory, premarketing notification system. This system protected the public health while serving the needs of industry and government. Generally, it was handled through straightforward correspondence between industry and the Food and Drug Administration. It focused on any real questions, and either produced a "no objection letter" from the agency or an industry decision not to go forward with a product.

This plan is still used in Canada, by our own Department of Agriculture, and in most of the rest of the world.

In the hearings which led to the 1958 amendment, however, FDA spokesmen kept reassuring Congress and industry that almost all packaging questions would continue to be resolved in the efficient, though informal, way that they had been handled previously. Despite these promises, SPI's testimony at the 1958 hearings, which I recall well, makes it abundantly clear that we were worried. We did not believe FDA's assurances. Most of all, we were fearful that the agency's determination to treat direct food additives and packaging materials identically would lead Congress into serious error.

The way we put it then was that "laws addressing food and intentional additives should not be indelicately applied to packaging components without careful deliberation." Our warning was even more prophetic than we thought. It is true that from 1958 until 1961 FDA kept its word and ran an informal, premarketing notification system through correspondence, at least for most packaging materials, those that presented no particular problem, which is the vast majority.

Industry gave the agency the data it needed, and FDA responded by concurring reasonably promptly in nonfood additive status for several hundred constituents of food packaging materials.

However, beginning in 1961, FDA decided to start tightening the screws. Its shift in approach had nothing to do with public health or any aspect of public health concern. Rather, as detailed in our written statement which we have submitted for the record—which I assume will be included—the change was based solely on its concerns about having to write too many letters. The fact is that there has never been a Food and Drug Administration seizure of a packaging material, nor has it ever been seriously contended that a packaging material has presented a public health problem.

Nevertheless, from 1961 until the present time, it has been virtually impossible to get FDA to concur in the nonadditive status of substances used in food contact surfaces.

Despite the absence of any public health problem, to warrant such burdensome regulation, FDA staffers estimate, of the 200 or so people working on food additives, about 85 percent of their time is spent on packaging materials or other indirect additives. I guess we are the ones that some of the previous speakers were talking about when they mentioned the fact that there needs to be some prioritizing so that so much money will not be wasted on such a minor problem.

In any case, earlier testimony has covered the scientific advances which have made the 1958 statutory approach obsolete.

But even without these advances in our ability to detect the migration of a few molecules, there would be a need for reform of the food safety laws to make the regulatory system for packaging consistent with its ultimate objective—a reasonable screening to assure that no public health problems are presented.

In our written testimony we have documented the history of when the indirect additives dilemma started and how far it has gone. What we are saying and what we submit our prepared testimony documents is the fact that grave misuses of the legislative and administrative processes have occurred, have been perpetuated with disastrous effect for the past 25 years, and should be corrected now.

Again to quote you, Senator Hatch, "Commonsense regulation is what is called for and what we need."

It may have been ordered by the courts through the 1979 decision in *Monsanta Company* v. *Kennedy.* Since I was a counsel in that celebrated case, which has been so much discussed here, I would ask permission to have a little three-page summary updating that case included as an attachment.

The CHAIRMAN. Without objection, we will add that at this point.

["The Monsanto An Copolymer Beverage Bottle Story" follows:]

The Monsanto An Copolymer Beverage Bottle Story

For more than a decade, Monsanto Company committed major resources toward the goal of developing a technologically superior, environmentally sound plastic container for carbonated beverages. Monsanto determined to make a plastic so inert that there would be no reasonable expectation of migration of the plastic into the food, *i.e.*, that it would not be a food additive as that term is defined by the Federal Food, Drug and Cosmetic Act. Monsanto succeeded, but market realities ultimately required that FDA agree that the bottle was not a food additive. Accordingly, from 1972 to 1974, Monsanto provided to FDA massive quantities of analytical evidence to support its own determination that no uncleared components of the bottle would migrate under the intended conditions of use.

Although the Agency agreed that there was no evidence of migration, it would not agree that the bottle was not a food additive, largely, we suspect, because of the high visibility of the product. In 1974, however, the Agency agreed that if Monsanto would permit the data it submitted to be handled as a Food Additive Petition, a responsive regulation clearing the bottle would be promulgated promptly because there were no safety concerns.

In November, 1974 Monsanto agreed to this procedure, and in February, 1975 a responsive regulation, then codified as Section 121.2629 (now § 177.1040) of the Food Additive Regulations, was promulgated.

Shortly thereafter, concerns arose regarding the toxicity of acrylonitrile (conveniently referred to as AN), one of the raw materials used to make the resin which was subsequently fabricated into the Cycle-Safe bottle. As a result of these concerns and a threatened "expose" by a well-known investigative reporter, on February 11, 1977 the Food and Drug Administration issued a press release, with no evidence whatsoever, stating that it believed the Monsanto bottle would not meet a newly-to-be-proposed interim limit on AN migration and that it planned to revoke the regulation permitting the use of the bottle. The rapidly-growing market for this container immediately collapsed, leading to the loss of over 800 bottle-manufacturing jobs in Monsanto plants and a corporate loss now estimated at $100 million; Monsanto reported $20 million dollars in lost earnings in 1977 alone.

During a court-ordered hearing in June 1977 and at a subsequent trial before the United States Court of Appeals in

March, 1979, FDA abandoned all pretense that the Monsanto bottle could not comply with the proposed AN migration limit. Rather, FDA shifted its ground and argued that although migration could not be detected with the best available analytical methods, this was irrelevant; instead, the Agency maintained that since AN was used to make the resin, some must remain in the bottle walls and, therefore, some quantity, no matter how minute, must migrate to the food.

Although the Court of Appeals in its November, 1979 decision soundly rejected this argument, clearance of the bottle remains to be achieved even in the face of evidence showing no migration with a method sensitive to less than 100 parts per trillion and sound, independently validated scientific evidence showing that migration really has ceased. The Agency has conceded in a June 1982 letter that safety is no longer an issue so we are hopeful about the final outcome. Even so, with luck, the FDA clearance process will have required from 1974 to 1983, involved huge financial losses, and perhaps irreparably damaged the market for the product.

Mr. **Heckman**. In many respects, we agree with some of what the consumer activist witnesses had to say about Monsanto, since they seem to agree that packaging materials with virtually no migration should be permitted, regardless of the Delaney clause.

Of course, when I say that we agree with what they say, I am talking about the substance of that principle. What I mean, of course, is that we agree that the Monsanto court said, in effect, that FDA should ignore undetectable or trivial amounts of unwanted substances.

It follows that it should also reinstate the clearance for the Monsanto bottle, which was withdrawn in 1977.

That brings me to the real point of mentioning the case. The fact is—and this points up our overall problem—4 years have passed since *Monsanto* v. *Kennedy,* and FDA is still sitting on the clearance Monsanto once had and has been seeking to reinstate since 1977.

This one case proves to us that a change must be mandated by the Congress. As Drs. Kennedy, Goyan, and now Hayes have indicated this week, the Food and Drug Administration has shown that it cannot accomplish what is needed—cannot maintain its credibility—without your legislative direction.

In our statement submitted for your record we have charted the sort of delays our industry's petitioners must expect in dealing with the inflexible requirements of the current law. The charts we submitted, and what everybody knows, show that time lags of 2 years or more to clear even an adhesive ingredient, which by regulatory definition is not expected to become a component of food, are not uncommon.

Because customers are not willing to wait 2 or more years for FDA clearances and because the cost to bring about such changes are excessive, you can be certain many safe products which would benefit consumers are never marketed. The loss has been serious.

The present statutory system has arrested innovation and forced the packaging industry in this country to lag far behind areas like Western Europe. Worst of all, this will continue indefinitely unless Congress acts.

Commissioner Goyan gave examples like the Brik Pak case to show how the present law breeds delay. Brik Pak, Monsanto, and stories like it, are legion. They are not rare; they are commonplace as far as packaging is concerned.

Time does not permit further detailing of our 20 years of frustration and disappointment here. We need congressional help. The packaging industry stands ready to do its part to bring about the remedial legislation of the type placed before the Senate in various forms in the last session.

Again, the plastics industry commends this committee for holding these hearings, for its patience in devoting its time to this subject, and for allowing us to participate.

Thank you.

[The prepared statement of Mr. Heckman and additional material supplied follows:]

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July 13, 1983

Ronald F. Docksai
Staff Director
United States Senate
Committee on Labor and
Human Resources
Washington, D.C. 20510

Re: Transcript

Dear Mr. Docksai:

Enclosed is a copy of my June 10, 1983 testimony that has been corrected in accordance with the instructions in your cover letter. Also enclosed is "The Monsanto AN Copolymer Beverage Bottle Story," which should be inserted on page 161 of my remarks.

Senator Hatch posed an additional question concerning whether current law stifles innovation. Both my oral testimony and the written statement submitted on behalf of The Society of the Plastics Industry, Inc. (SPI) support the view that the law does stifle innovation in food packaging. To expand on this, I am enclosing two letters representative of the difficulties faced by the industry. I have requested additional examples and will submit them to the Committee at some later time.

If I can be of any further assistance, please let me know.

Cordially yours,

Jerome H. Heckman

Jerome H. Heckman

Enclosure

MR. HECKMAN

ADDITIONAL QUESTIONS FOR INDUSTRY PANEL PREPARED BY SENATOR HATCH

1) During the hearing, several witnesses discussed the effect of current law on innovation. In your opinion, does current law stifle innovation? How? Please provide examples to support your conclusion?

The BFGoodrich Company
500 South Main Street
Akron, Ohio 44318

Address Reply To:
Dept. 0020
Bldg. 5-H

May 26, 1983

Mr. Jerome H. Heckman
Keller and Heckman
1150 - 17th St., NW, Suite 1000
Washington, D.C. 20036

Dear Mr. Heckman:

This is in response to your May 18, 1983 letter concerning the Senate food safety hearings.

In the past several years the BFGoodrich Company had decided not to pursue FDA clearance for a number of products due to either one or a combination of: uncertainty, costs, and the length of time involved. This has been particularly true with substances that have limited food contact applications.

For example, we have had copolymers which were improvements over currently regulated copolymers, but whose specific composition was not regulated although they were composed of monomers currently regulated for other copolymer compositions, thus necessitating a petition to amend one or more regulations. Clearance was not pursued, either because our customer was not willing to wait the typical two or more years from conception of the product until FDA clearance might be obtained, or the costs involved could not be justified.

In another instance we explored additional clearance for use of one of our products currently regulated for very limited application in food contact articles. Past 90-day toxicity studies in two species (rat and dog) showed no effects at the highest level fed, 10,000 ppm (1% of diet). Past extraction studies, under exaggerated conditions of time and temperature, had shown that less than 0.5 ppm from contact with acqueous foods, and less than 1 ppm from contact with fatty foods, would be added to the diet if all foods were packaged in an article containing this ingredient. Clearance was not pursued since the cost of additional migration and toxicity tests were prohibitive.

Even when obtaining an advisory opinion, the costs and time required can be substantial. Several years ago we explored obtaining FDA clearance for one of our copolymers. We were verbally informed there was no need for a petition to amend the desired regulations since the subject copolymer was already cleared by the description of a currently regulated copolymer. Based on the chemistry involved, we relied on this opinion to assure our customers that our product was indeed cleared for the desired use. However, when the USDA requested a written opinion from the FDA, the FDA would not provide a written statement without experimental data to demonstrate what they had originally told us. To resolve the situation required one year and an expenditure of approximately $15,000 in testing costs. Meanwhile, untold costs were experienced by our customers and ourselves due to the confusion and lack of clear acceptance of our product.

I hope these examples will be of help. It is difficult to cite other examples of prohibitive costs, uncertainty and exhorbitant time without revealing proprietary information.

Very truly yours,

W. C. Bachtel

W. C. Bachtel
Toxicologist

v

cc: M.N. Johnson, M.D.
H.W. Dietz, M.D.

June 13, 1983

Mr. Jerome H. Heckman
Attorney at Law
Keller and Heckman
1150 - 17th Street, N.W.
Washington, DC 20036

Dear Jerry:

While listening to your discussion of annecdotal information related to the FDA and the delay of bringing new materials and packages to the marketplace, I thought about the following "epic" of which I was a participant. One of my first assignments after joining Continental was to work with the FDA in obtaining approval for a retortable pouch. While discussing past work assignments recently, one of my employees told me this was also a part of his first assignment when he joined Continental 21 years ago.

The retortable pouch was a truly innovative approach to bringing new materials and concepts together in such a way that the new container would be lighter weight, shelf-stable and appealing to the consumer, as well as less costly and more energy efficient for the manufacturer and retailer. The utility and appeal of this package was so great that its development was encouraged by the U.S. Army and was ultimately selected by NASA as the package for the food consumed by the astronauts on the early space flights and was the package used on the lunar flights.

Continental worked diligently for more than 15 years to obtain FDA approval for the package. Over the years, the concerns of the FDA were removed one-by-one and, ultimately, only the approval of the adhesive system remained. After continued delays and requests for additional data and many millions, R&D dollars, the division responsible for the retortable pouch was finally sold and the project scraped.

The retortable pouch was a packaging concept which arrived before its time. It was awarded major packaging innovation awards, including the package of the year award. The retortable pouch was accepted by the Army for our troops, used by NASA to feed our astronauts, traveled to the moon and our space station, but never made to the local grocercy shelf because of the slow pace of FDA approval.

Sincerely,

William Hoyle

W. C. Hoyle
Director - Materials Development &
Analytical Services

WCH/mjj

STATEMENT OF

JEROME H. HECKMAN

on behalf of

THE SOCIETY OF THE PLASTICS INDUSTRY, INC.

before the

UNITED STATES SENATE COMMITTEE ON
LABOR AND HUMAN RESOURCES

concerning the

NEED FOR FOOD SAFETY AMENDMENTS

June 10, 1983

I. INTRODUCTION

My name is Jerome H. Heckman, of the Washington, D.C. law firm of Keller and Heckman. I am General Counsel for The Society of the Plastics Industry, Inc. ("SPI" or "the Society"), and am presenting this Statement on behalf of the Society. It is a privilege and pleasure to testify before this Committee, discuss the need for food safety law amendments, and urge the prompt enactment of necessary changes.

By way of background, the Society represents some 1,200 member companies and is the major national trade association of the plastics industry. Its membership represents over 95% of the production and about 75% of the sales of plastics materials in the United States. SPI has been the spokesman for the plastics industry in seeking reasonable supervision of food packaging and cautioning against over-regulation in this area. To a large extent, comments filed by SPI with the Food and Drug Administration (FDA), the National Academy of Sciences (NAS) and other bodies have been further elaborations on the basic theme of SPI's testimony at the congressional hearings[1/] which led to the passage of the Food Additives Amendment of 1958 (hereinafter "1958 Amendment").[2/] SPI's interest focuses primarily on issues relating to food packaging.

[1/] Food Additives: Hearings on Bills to Amend the Federal Food, Drug, and Cosmetic Act Before a Subcomm. of the House Comm. on Interstate and Foreign Commerce, 85th Cong., 2d Sess. (1958)(hereinafter "1958 Food Additives Hearings").

[2/] Pub. L. No. 85-929, 72 Stat. 1784 (1958).

There is a patent need for change; a change that will remove an unnecessary regulatory burden, liberate arrested innovative potential, and continue to assure that our food supply is protected by safe state-of-the-art packaging. There is every reason for Congress to distinguish between the regulation of direct and indirect additives so that what is of critical importance can be prioritized, and what is of lesser or no consequence can be evaluated quickly without excessive expenditures of government and industry time and money.

In considering what follows, it is helpful to bear in mind the underlying factors which have prompted us to participate in this legislative process. We view it as a long-overdue opportunity to correct a very obvious case of burdensome overregulation. During its 25 years of existence, the Food Additives Amendment of 1958 has intruded into the packaging and equipment areas in such a way as to inhibit innovation and saddle the industry with regulatory procedures not needed to assure safety. Yet, there has never been an instance indicating--much less demonstrating--that a packaging material has caused any public health problem.3/ We are unaware of any FDA case aimed at condemning or seizing food because the packaging material presented a health hazard. Moreover, FDA staff members who deal with indirect additives have informally stated that, because of its structure, the regulatory system governing food-packaging materials is essentially unenforceable and useless except for self-policing by manufacturers.

3/ Frawley, J.P., A Reasoned Approach to Regulation Based on Toxicologic Considerations, 23 Food Drug Cosm. L. J. 260(1968).

II. SUMMARY

Under the Federal Food, Drug, and Cosmetic Act (Act), the term "food additive" constitutes a single category for regulating substances which come into contact with food. The term includes both substances intentionally added to food, and substances that are not intentionally added, but that contact food and are reasonably expected to migrate into food. Substances in this latter category are sometimes referred to as "indirect additives." They include food packaging materials and other substances which come into contact with food during its handling, such as conveyor belts in a food processing plant, if it is reasonably expected that the substance will become a component of food. Because only one statutory category exists for these different additives, they are all subject to the same food additive approval process.

The current approval system, which mandates a rulemaking procedure in all cases, is unnecessarily expensive and time consuming. The present system simply does not make sense for the vast majority of food-contact substances and is a waste of both FDA and private resources. Indeed, change is clearly needed to correct a glaring defect in the current law. In many instances, packaging material manufacturers and food packagers will refuse to utilize a substance unless it is subject to an FDA regulation. Indeed, we have occasionally encountered situations when FDA clearance has been demanded by the customer even though a non-food-contact application was involved. Yet, at the same time, because of the long delay, expense and burden imposed by current law, food additive petitions are not filed for many useful substances even when it is clear that such substances pose no risk to human health. Therefore, we urge the enactment of premarket notification provisions to ease the burdens and delays associated with marketing a new food-packaging material.

Justification for differing statutory treatment of direct food additives and food-contact substances is based on several factors. These include the history of FDA packaging regulation, the different regulatory issues that packaging presents, and scientific advances over the last 20 years that make the current statutory language conflict in practice with its intended purpose.

The Food Additives Amendment of 1958 defined a food additive as any substance the intended use of which "results or may reasonably be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristics of any food . . . ." Consequently, to determine whether a substance that comes into contact with food is a food additive, one must decide if the substance may reasonably be expected to become a component of food under intended conditions of use. Over the years, FDA's view of this definitional question and the resulting regulatory response have followed an inconsistent course.

Initially, FDA routinely responded to requests for its concurrence in non-additive status when satisfactory data were presented indicating no reasonable expectation of migration. Then, in the early 60s, FDA adopted the position that if a company conducted extraction studies, the testing must have been predicated on an expectation of migration, and, therefore, the product was a food additive regardless of the test results. By conservative estimate, this FDA position generated hundreds of food additive petitions on pre-1960 "non-additives" and added unnecessary pages to the Code of Federal Regulations. It was not until 1970 that the Agency ultimately withdrew from the position embraced in 1960. Even so, few, if any, letters of concurrence in non-additive status were issued.

In 1977, the Agency did another about-face. It maintained that a container material would be a food additive merely because the packaging had contact with food. Of course, under this reasoning, all containers, packages and other food-contact substances would be regulated as food additives, a result clearly not intended by the 1958 Food Additives Amendment.

Fortunately, this position was rejected by the United States Court of Appeals for the District of Columbia Circuit in Monsanto v. Kennedy.[4/] In that case, the court of appeals stated that FDA must determine with a fair degree of confidence that a substance migrates into food before it becomes a food additive. The Monsanto court also held that FDA has latitude to find migration "insignificant," based on the administrative discretion to deal appropriately with de minimis situations.

Although this opinion is three and one-half years old, FDA has yet to implement a policy which actually exempts insignificant migratory components. Whatever solutions may theoretically be said to derive from the Monsanto decision, none has been realized in fact. FDA and industry continue to waste staff and financial resources on food additive petitions for food-contact substances for which the present statutory procedures are inappropriate.

Separate statutory treatment for food-contact substances also recognizes the different questions that regulation of these substances presents. When substances are directly and intentionally added to food, there is little if any

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[4/] 613 F.2d 947 (D.C. Cir. 1979).

disagreement concerning their presence or the quantities involved. The only issue to be decided is whether the additives have adverse health effects. For packaging material and other food-contact substances, however, the controlling question is often whether any migration into food occurs and, if so, how much material migrates. If there is no detectable migration with an adequately sensitive test method, toxicological issues are essentially irrelevant, as the scientific community and countries like Canada have continuously recognized. Occasionally, FDA has endorsed this concept but the Agency has not applied it in practice. Because the initial questions facing FDA are distinctly different for direct and indirect additives, separate treatment is warranted.

A final reason for separate treatment of food-contact substances arises from scientific advances. In 1958, analytical chemists were generally unable to detect concentrations of substances of less than several parts per million (ppm) with any reasonable degree of certainty. If tests designed to exaggerate actual conditions of use showed that a substance migrated into food-simulating solvents, the level at which it could reasonably be expected to be present in food might be in the range of a part per million or more. In stark contrast, techniques are presently available to detect a few parts per trillion (ppt) for many substances, and almost all laboratories can detect substances in the range of parts per billion (ppb).

Looking to the future, advances in analytical chemistry promise the ability to detect single molecules or atoms of substances. Such advances make it possible to find substances migrating from food packaging to food in vanishingly small amounts that are insignificant in terms of human health. Thus, continued application of the curent statutory language will generate more problems unworthy of intense regulatory attention.

There is a pressing need for a simplified procedure to approve safe food-contact substances. At the present time, it can take three or more years between the filing of a food additive petition and final approval. Often this process takes even longer. Because food-packaging materials are treated like direct additives, FDA has been forced to misallocate or waste its administrative resources in the food area. One FDA official has estimated that 85% of the Bureau of Foods' food additive work is spent reviewing packaging and that these statutory obligations have precluded the Bureau from focusing on real problem areas.

Although no legislation is before this Committee, we note that draft bills by the Sub-Cabinet Council Working Group on Food Safety Reform, this Committee's staff working draft of April 20, 1982, and legislation introduced during the last Congress all provided the option of a self-executing premarket notification system as an alternative to the much more formal petition-regulation system. This represents a broad consensus that such a change would improve the regulatory system, adapt it to changing scientific realities, and continue to protect the public health.

III. STATUTORY AND REGULATORY HISTORY

A. FDA Review of Food Contact Substances Before 1958

Until 1958, the Act did not require premarketing clearance for any type of packaging material. Nor were there any known problems that indicated a need to clear "indirect additives." Nonetheless, long before consideration of any specific legislation to require FDA review of food-packaging materials, food industry purchasers of containers or equipment used in food-contact applications required some reasonable assurance that the products would not present any undue hazard to the public health or create any liability in the ordinary course of business. Food packagers and processors had to be convinced that the package could not reasonably be expected to adulterate the food or otherwise violate the Act.[5/] These prospective customers were keenly aware of the necessity for protecting themselves against potential liability resulting from the use of food-contact materials that might in some way contaminate foods.

It was readily apparent to both the packaging materials supplier and potential customers that one way of assuring statutory compliance would be to secure a written opinion by the appropriate federal authorities concerning the safety of a material or component for an intended use. Thus, submitting data to federal officials and soliciting their reactions was a completely voluntary matter, done primarily to satisfy customers of packaging suppliers. However, the practice of soliciting a response from FDA was exceptionally widespread; almost all responsible companies followed it long before 1958.

Customarily, a company submitted its data, perhaps after conferences with appropriate officials, and received advice as to whether there was any objection to the proposed use, or whether additional data might be required. If more information was deemed necessary, it was supplied. The amount of data

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5/ 21 U.S.C. SS 301 et seq.

depended on the precise circumstances relevant to the specific packaging material. The important point is that FDA was being asked to examine only a specific product made by a specific manufacturer who was before the Agency and ready to supply all the information required to assure safety. In contrast to the present system, FDA was not attempting to devise broad regulations concerning the generic use of a packaging substance. Because of the specific nature of the inquiry, obtaining "no objection" letters from FDA was not an inordinately time-consuming or expensive matter. Usually, delays were attributable to a genuine need for additional scientific information.

Once questions bearing on safety were resolved, the manufacturer received one or more letters from FDA or the Meat Inspection Division (MID) of the Department of Agriculture (USDA)(now the Product Safety Branch of the Food Ingredient Assessment Division of USDA's Food Safety Inspection Service). A typical MID letter advised that a product was "acceptable for use in federally-inspected meat plants." An FDA response indicated that the Agency "would raise no objection" to the use of the product in food-contact applications.

The great virtue of these informal proceedings was the prompt production of a basis for allaying customer fears about possible government agency enforcement action. Indeed, many view this prior practice as better than the present system employed by FDA.

Today, this type of procedure is still employed by the Department of Agriculture when a material is to be used in a federally-inspected meat or poultry plant. Unfortunately, however, in just the past four years or so, USDA has tied its approval process to the current FDA regulatory scheme so that occasional confusion and delay are encountered at USDA. Even so, securing

USDA clearances generally takes far less time than that required to obtain an FDA regulation. In November, 1982, USDA published a proposed rule to clarify that USDA letters are not a mandatory premarket approval process and that letters from materials manufacturers assuring compliance with applicable Food Additive Regulations are sufficient.[6/]

Incidentally, the pre-1958 approach is used for essentially all food-contact applications in Canada since Canadian law exempts packaging materials from the type of regulation imposed on direct food additives.[7/] The same is true for most of the rest of the world including the European Economic Community nations.

B. Food Additives Amendment of 1958

1. Legislative History

In large part, the Food Additives Amendment of 1958 flowed from the so-called Delaney Hearings held between 1950 and 1952.[8/] To the best of our

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[6/] 47 Fed. Reg. 50,914 (Nov. 10, 1982).

[7/] See generally, Canadian Food and Drug Regulations, section B.01.001(d)(v). The Canadian Health Protection Branch has recently approved the use of food packaging materials containing acrylonitrile monomer residues so long as there is no detectable migration to food using the "official method." It is our understanding that the official method for determining acrylonitrile in food (as distinguished from food-simulating solvents) has a sensitivity of about 15 ppb ± 50%, depending on the particular food under analysis. Information Letter No. 607, Canadian Health Protection Branch (Sept. 21, 1981); Food Chemical News, p. 1 (Nov. 9, 1981)(copies attached in Appendix D).

[8/] Hearings Before the House Select Comm. to Investigate the Use of Chemicals in Foods and Cosmetics, 81st Cong., 2d Sess. and 82d Cong., 1st and 2d Sess. (1950-1952); see H.R. Rep. No. 2356, 82d Cong., 2d Sess. (1952).

knowledge, the entire record of the Delaney Hearings and FDA's statements concerning a need for new legislation that would require formal agency clearance prior to marketing dealt only with substances directly and intentionally added to foods. Unfortunately, this avowed necessity for new regulatory authority to control the intentional and direct addition of various substances to food resulted in legislation that regulated packaging and processing materials in precisely the same way as substances deliberately added to food.

I recall quite vividly an appearance made by the Chairman of the Society's Food Packaging Materials Committee urging that the 1958 Amendment not apply the same law to both direct additives and food-packaging components. On behalf of the Society, he recommended the passage of a bill that would make "mandatory the advance submission of pretesting data to the FDA prior to the marketing of new substances . . ." through a system of premarket notification. He stated that laws addressing food and intentional additives to food should not be "indelicately applied to packaging components without careful deliberation." The industry feared that a rulemaking system for food additives would prove cumbersome and misguided when applied to packaging materials and that it would undoubtedly stifle innovation, require an immense increase in FDA's budget, create delay in securing regulatory approval, and ultimately limit manufacturer and consumer choices for food packaging.[9/]

[9/] 1958 Food Additives Hearings at 149-153. Others expressed similar misgivings. 1958 Food Additives Hearings at 207-208 (National Canners Association), 410 (Waxed Paper Institute), 444 (American Paper and Pulp Association), and 482-488 (Adhesives Manufacturing Association); see also, pp. 494-495 (Supplemental SPI Statement).

Unhappily, there was little discussion of the potential impact of the legislation on the so-called indirect additives. It is with some personal regret that I confess we were unable to attract congressional attention to the problems inherent in the approach taken under the 1958 Amendment. The past twenty-five years have proven that industry fears concerning the effects of a premarketing clearance system were justified. Indeed, experience teaches that our fears were understated in the 1958 Hearings. As far as food packaging is concerned, the 1958 Amendment produced needless impediment.

2. Statutory Plan

The Food Additives Amendment of 1958 added two signficant provisions to the Act concerning FDA regulation of food packaging. First, it added a definition for "food additive." Section 201(s) of the Act defines a food additive as "any substance the intended use of which results or may reasonably be expected to result, directly or indirectly in its becoming a component . . . of any food (including any substance intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food . . .)" except for substances that are generally recognized as safe by qualified experts or are prior-sanctioned.[10]

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[10] Section 201(s) of the Act, 21 U.S.C. § 321(s) provides:

> The term "food additive" means any substance the intended use of which results or may be reasonably be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristics of any food (including any substance intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food; and including any source of radiation intended for any such use), if such substance is not generally recognized, among

Secondly it declared, in section 409 of the Act,[11] that any food additive shall be deemed unsafe unless it is used in conformity with a regulation issued by FDA or an investigational use exemption. To support promulgation of a regulation, the manufacturer must file a petition with FDA containing the necessary safety information. Based on this submission, the Commissioner makes a determination on the safety of the packaging material under intended conditions of use. This includes an evaluation under the prohibitions of the

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[Footnote 10/ continued.]

> experts qualified by scientific training and experience to evaluate its safety, as having been adequately shown through specific procedures (or, in the case of a substance used in food prior to January 1, 1958, through either scientific procedures or experience based on common use in food) to be safe under the conditions of its intended use; except that such term does not include—
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> (1) a pesticide chemical in or on a raw agricultural commodity; or
>
> (2) a pesticide chemical to the extent that it is intended for use or is used in the production, storage, or transportation of any raw agricultural commodity; or
>
> (3) a color additive; or
>
> (4) any substance used in accordance with a sanction or approval granted prior to the enactment of this paragraph pursuant to this Act, the Poultry Products Inspection Act (21 U.S.C. § 451 and the following) or the Meat Inspection Act of March 4, 1907 (34 Stat. 1260), as amended and extended (21 U.S.C. § 71 and the following); or
>
> (5) a new animal drug.

[11] The text of Section 409 of the Act, 21 U.S.C. § 348, is reproduced in full in Appendix B to this Statement.

Delaney Clause, embodied in section 409(c)(3) of the Act.[12] In addition, the rulemaking encompasses consideration of the probable consumption of the additive, the cumulative effect of the additive in the diet and other safety factors.[13]

The statute directs FDA to issue a regulation authorizing use or an order denying the petition within 90 days after the petition is filed. FDA may extend the 90-day period an additional 90 days if it deems it necessary to study the petition. The regulation or order must be published, objections may be received and public hearings held. Judicial review may follow.

C. FDA Regulation of "Indirect Additives"

1. 1958-1961: Age of Reason

After passage of the 1958 Amendment, FDA initially exercised its new regulatory authority over packaging materials in a reasonable manner. Agency spokesmen advised manufacturers that if extraction studies indicated no migration, then the packaging material was not a food additive.[14] Often, packaging manufacturers would submit the results of extraction studies and obtain formal concurrence from FDA that the packaging was not a food additive or presented no food additive problem. Indeed, FDA rejected some food additive petitions for packaging materials on the basis that extraction studies indicated no migration with methods sensitive to 1 ppm. The Agency simply concluded that the packaging was not reasonably expected to become a component of food and was not a food additive.[15]

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[12] 21 U.S.C. § 348(c)(3).

[13] Section 409(c)(5) of the Act, 21 U.S.C. § 348(c)(5).

[14] Food Packaging Under the Food Additives Amendment—What Needs to be Done, pp. 2,3. Paper presented by Mr. Checchi (then Assistant to Deputy Commissioner Harvey) at the 14th Annual Paper and Plastics Conference, Chicago, Illinois, September 22, 1959.

2. 1960s: Testing Means There Is "Migration"

FDA's reasonable interpretation of the term food additive as applied to packaging substances began to erode within two brief years. In 1960, for reasons unrelated to public health and safety, the Agency abruptly abandoned its practice of formally concurring in non-additive status where extraction studies indicated an absence of migration.

Industry maintained that FDA had an obligation under its procedural regulations to provide clear advice on the status of products under the 1958 Amendment. In response, the Agency's attorneys stated that if a company went to the trouble of conducting extraction studies, the company must have believed

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[Footnote 14/ continued.]

> Once the extraction studies are completed, you will find yourself confronted with one of two possibilities. There may be no expected migration of any substance to food. If so, you're home free. The packaging material you have tested is not subject to the Amendment, except in the unlikely event that it otherwise affects the characteristics of the food contained in it.

15/ Color Additives, Hearings on H.R. 7624 and S. 2197 Before the House Comm. on Interstate and Foreign Commerce, 86th Cong., 2d Sess., 104-05 (1960).

that some or all of its product might reasonably be expected to become a component of food, and, therefore, the product or its components are legally food additives even though the extraction studies detect no migrating materials.[16]

Under this theory, there really could be no meaningful exemption for packaging materials that did not migrate to the food. As a practical matter, no responsible manufacturer would conclude that a food-contact substance is not a food additive without performing some type of extraction study.

While we now assume that FDA no longer formally embraces this theorem, the philosophical outlook it evidenced continues. Despite repeated requests by industry and the passage of 20 years, FDA has never firmly quantified the meaning of the statutory phrase "may reasonably be expected to become a component of food." Nor has it established workable procedures for concluding that a substance may not be expected to become a component of food. As the sensitivity of analytical methods for detecting trace migrants from

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[16] This FDA legal theory was first formally explained in an address given by the then Deputy Commissioner of FDA, John L. Harvey, at Rutgers University on January 18, 1962. In pertinent part, Deputy Commissioner Harvey's explanation was as follows:

> We came to the conclusion that we had opened Pandora's box and had better find a way to close it before the situation got completely out of hand. We therefore reevaluated our position after consultation with our legal counsel and came to the conclusion that basically, if there was enough reason to run extraction studies on packaging or equipment materials, why shouldn't it be concluded that it would be reasonable to expect that the substances involved would, in fact, become a part of the food? Since the law refers to 'reasonably to be expected' we then began to advise those who asked that we were not in a position to give them a letter which would absolve their

packaging material improves, the burden of FDA's policy of vagueness will continue to be grossly magnified.

3. Early and mid-1970s: Test to Equilibrium

More recently, FDA scientists began advising manufacturers in a few cases that a packaging material would not be considered a food additive if no detectable extraction is observed with a validated analytical method when the material is tested "to equilibrium" in accordance with the Agency's guidelines.[17/] These official guidelines were intended to provide an estimate of the maximum amount of a packaging substance that might migrate to foods under intended conditions of use. Thus, FDA requires that the testing exaggerate time, temperature and exposure conditions. On rare occasions, FDA has reviewed a manufacturer's data indicating no migration based on extraction studies performed under simulated conditions of use and issued letters stating that "no food additive problem" was presented. Although this represents an enlightened approach compared to the 1962 FDA position, it has not been without substantial defects; worse, at present there is no way of knowing whether this policy is

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[Footnote 16/ continued.]

> product from any responsibility under the Food Additives Amendment but instead suggested that they file petitions. That is the present status of this item.

Harvey, Food Additives and Regulations, 17 Food Drug Cosm. L. J. 275 (1962).

17/ FDA Guidelines for Chemistry and Technology - Requirements for Indirect Additive Petitions (March 1976) reproduced in CCH Food Drug Cosm. L. Rep. ¶ 56,068.12 at pp. 56,043-56,049.

viable. Such letters are not issued routinely. Moreover, there are no published criteria for a determination of additive or non-additive status.

As an example, for one product FDA stated that it would not agree to a "no migration" position unless testing had been conducted for so long a time and at such a high temperature--no matter how unrelated to intended conditions of use--that some migration under some condition is shown. FDA advised the packaging manufacturer in that case that until detectable migration of a suspected carcinogen is found, one cannot say that the extraction work has been conducted "to equilibrium." Therefore, FDA could not conclude that there was no reasonable expectation of migration. Although the rhetoric may have changed since 1962, the misguided reasoning has not.

4. Recent Regulation Predicated on Theoretical Diffusion

In the context of an essentially adjudicatory proceeding in 1977, FDA chose not to rely on measurements or sound projections of migration as a basis for regulating packaging. Rather, it adopted a position that would have based the regulation of packaging components on a principle derived from the second law of thermodynamics. That principle predicts some migration, however minor, when any two substances come into contact. In other words, FDA asserted jurisdiction based on the theoretical diffusion of the packaging components into the food as opposed to regulating packaging components as food additives only when there is significant detectable migration into food under intended conditions of use.

This situation arose after an acrylonitrile copolymer container was developed from which no migration could be detected using the best test then available, one sensitive to 10 ppb. FDA insisted on estimating migration from the new bottle, although none was detectable, by extrapolating from data on an earlier bottle containing higher levels of residual acrylonitrile monomer and from which there was detectable migration. In essence, it invoked the second law of thermodynamics to claim that there must be some migration, albeit undetectable, and that the container material was therefore a food additive. Of course, under this reasoning, all containers, packages, and other food-contact substances would be regulated as food additives, a result clearly not intended by the 1958 Food Additives Amendment.

After preliminary administrative proceedings and a trip to the court of appeals, FDA concluded that acrylonitrile was a food additive even without test evidence of migration. The United States Court of Appeals for the District of Columbia Circuit rejected this position in Monsanto Co. v. Kennedy.[18/] There, the court held that FDA must determine with a fair degree of confidence that a substance actually migrates into food in more than insignificant amounts before it becomes a food additive, and that FDA has latitude to find migration "insignificant."

Given this opinion, we expected that FDA would promptly clarify the status of the acrylonitrile bottle material in a favorable decision. While the court's opinion was issued in November 1979, no FDA action came until June

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[18/] 613 F.2d 947 (D.C. Cir. 1979).

1981, some 19 months later. Even that action was a hypertechnical rejection that did not settle the case.

5. Time Required for FDA Clearance

Under existing section 409(c)(2), FDA is required to act on a food additive petition within 90 days, although it may extend this period an additional 90 days, if needed, for a total time of six months. Although the statutory mandate is clear, the time limits are meaningless in practice.

The number of petitions filed each year for indirect food additives is hardly overwhelming. For the calendar years 1977 to 1982 the number of petitions filed annually ranged from a low of 13 in 1978 to a high of 47 in 1982. Yet, at the end of each year, between 46 and 85 petitions were still pending. At present, over 73% of the pending petitions have been pending in excess of the six-month statutory time limit.

Based on statistics more fully set forth in Appendix A to this Statement, averages over the 1977-1982 period show that about 55% of the petitions will be pending after one year, and 37% will be pending over two years. Approximately 24% are still pending three years after filing.

Although these figures represent unacceptable delay, they understate the actual amount of time the petitions have been before the Agency. When a manufacturer wishes to obtain FDA approval for an indirect food additive, it is common practice to meet with the appropriate Agency personnel to discuss a draft food additive petition. The draft is then modified in light of informal FDA comment.

Because of the difference between the official filing date and initial agency contact or submittal, determining the total actual time a petition has been pending is difficult. Thus, the figures presented here and in Appendix A most certainly understate the length of time necessary to obtain FDA approval. The real situation is worse. Certainly, some delay must be attributable to petitioners who do not respond to FDA requests for clarification or additional information.[19/] However, there is something drastically wrong with a system where the time limits are met for about one case out of four.

D. Changes in Analytical Techniques

The last twenty years have witnessed a vast change in the analytical techniques available to detect the migration of packaging components into foods. In 1958, analytical chemists were generally unable to detect substances in less than several parts per million with any reasonable degree of certainty. Thus, if a substance was found to migrate into food-simulating solvents in tests designed to exaggerate actual conditions of use, the substance might reasonably be expected to be present in food in the range of a part per million or more. In contrast, techniques are presently available to detect parts per trillion of many substances and almost all laboratories can detect substances in the range of parts per billion.

Looking to the future, the 1981 Nobel Prize in physics for advances in laser spectroscopy promises the ability to detect single molecules or atoms of

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19/ In some cases, the manufacturer's data are not accepted for reasons that can at best be characterized as picayune. FDA staff members often require that generally accepted principles be re-proven in each specific case.

substances.[20] Such advances may make it possible to find substances migrating from food packaging to food in amounts so minute that they are almost incomprehensible and clearly insignificant in terms of human health. Thus, continued application of the current statutory language in the face of scientific advances will only generate more problems unworthy of regulatory attention.

FDA publicly addressed the dilemma presented by improved analytical techniques in the late 1960s. This FDA consideration, an implicit recognition of the need to distinguish food-contact substances from other food additives, led to the Ramsey proposal, named after L. L. Ramsey, then the Assistant Director of Regulatory Programs in FDA's Bureau of Science. Under this proposal, the indirect Food Additive Regulations would have been amended to permit the use of most substances without the promulgation of regulations where the level of migration did not exceed 50 ppb (0.05 ppm).[21] If such a policy had been

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[20] The Washington Post, Oct. 20, 1981, at A1 and A14, col. 2.

[21] In a speech given on November 4, 1969 before the National Technical Conference of the Society of Plastics Engineers, Mr. Ramsey described the proposal as follows:

> This in-house proposal would amend the regulations to permit the use of substances (except heavy metals, carcinogens, and other substances that have been demonstrated to produce toxic reactions when present at levels of 40 ppm or less in the diet of man or animals) in food packaging materials and other food contact surfaces as follows:
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> 1. As components of food-contact articles provided any substance so used contributes no more than 0.05 to the contacted food;
>
> 2. As components of articles for use in contact with dry, non-fatty food;

adopted, the course of food packaging regulation might have been significantly improved. Unfortunately, the Ramsey proposal was never adopted, and the present unsatisfactory situation continues.

The history of the Monsanto case, cited above, also provides an apt illustration of the dilemma posed by increasingly sensitive analytical techniques. At the time of the administrative proceedings in the Monsanto case, quantities could be detected with an acceptable degree of confidence in parts per billion. By the time the case reached the court of appeals new techniques could detect concentrations of 0.1 ppb (100 ppt). Techniques are presently being developed to detect very low parts per trillion.

Detection at these levels may reveal a potential for truly insignificant migration presenting no health risk. (Remember, the testing is done under a progression of exaggerative conditions.) This is so even though the "migrant" may be a carcinogen. For example, using conservative methods which tend to overstate the potential incidence of cancer from exposure to packaging components that may migrate, several respected scientists calculated the risk that would have been presented by one type of acrylonitrile beverage container. Their estimates placed the odds against an individual suffering an early fatality

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[Footnote 21/ continued.]

3. As components of articles intended for repeated use in contact with bulk quantities of food;
4. As components of defoaming agents employed in the manufacture of paper and paperboard intended for use in contact with food.
5. As components of food-packaging adhesives.

between 3.5 in a billion (3.5×10^{-9}) per year and one in a trillion (1×10^{-12}) per year.[22]

To put these figures in perspective, please recall that they represent a worst-case estimate. The actual incidence is likely to be zero, but it will not exceed the risk figure. Moreover, risks on the order of one in ten billion (1×10^{-10}) correspond roughly to a potential for about one excess cancer in the country each century. Certainly, such a risk level does not merit decisional significance in any reasonable regulatory system. Indeed, the actual individual risk of early fatality we face from other causes is much greater. (Falls: 9 in one hundred thousand; air travel: 9 in one million; lightning: 5 in ten million.)

The present version of the acrylonitrile beverage container sought to be marketed would present even less of a risk; it presents no risk at all. This admittedly remarkable statement can be made because the level of residual acrylonitrile monomer remaining in the bottle is so low that, because of the energy that would be needed to release the monomer, one can say the wall of the

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22/ Professor Richard Wilson of Harvard University, a well-known authority on risk assessment, testified at the FDA hearing on AN/S copolymer beverage containers that using the extremely conservative linear method for extrapolating the cancer incidence observed in laboratory animals to humans, the individual risk of early fatality from consuming beverages in an AN/S copolymer beverage container was no higher than 1 in 290 billion (3.5×10^{-9}) per year. Testimony of Professor Wilson, FDA Docket No. 76N-0070, Exhibit M-90, p. 32.

Also testifying at this FDA hearing, Allan W. Dickinson, a Fellow in Statistics at Monsanto Company, applied the Mantel-Bryan risk extrapolation model to the interim data of the chronic rat study and projected an annual cancer risk to humans of less than one in a trillion (1×10^{-12}/per year). Testimony of Allan W. Dickinson, FDA Docket No. 76N-0070, Exhibit M-88, p. 3.

container acts as a prison that prevents migration.[23] Still, no FDA clearance has been given. Stated otherwise, the Monsanto decision may have solved the packaging problem as some leading commentators have said but FDA's actions in the three years since the decision belie this.

Reflecting the pressure of scientific reality, knowledgeable FDA officials have rejected the search for zero or absolute safety where the existing food laws do not force the Agency to act otherwise.[24] The mathematical concept of zero is distinct from what is normally understood when we refer to the presence or absence of a substance in the real world. As the Monsanto court recognized, FDA must be authorized to disregard insignificant amounts if our regulatory system is to be rational. Advancing technology forces us to recognize this and statutory plans that demand that "zero" be treated as a number instead of the relative concept must be amended correspondingly.

23/ More precisely, acrylonitrile monomer is an intermediate product that is converted into acrylonitrile polymer. The monomer is a suspected human carcinogen, while the polymer is an inert, safe substance. After the monomer is polymerized, that is, converted to a polymer, some monomer remains as an undesired residue. In the container mentioned in the text, the level of residual acrylonitrile monomer is so low that the monomer is trapped in the polymer matrix and no migration takes place.

This conclusion does not offend the second law of thermodynamics discussed previously. That law predicts some migration, however small, when two substances come in contact but does not consider how long a time might be required to achieve it. Because the bottle wall acts as a barrier between the monomer and the food, the time required for even infinitesimal migration would be extended to perhaps centuries or eons. Thus, no migration would need to occur under this scientific principle in any finite time period.

24/ An instructive speech by Sanford A. Miller, Director of FDA's Bureau of Foods, is attached as Appendix C. Another example is the Agency's decision to permit the use of lead acetate in hair dyes. 46 Fed. Reg. 15,500 (Mar. 6, 1981).

FDA's proposed policy for regulating carcinogenic chemicals in food and color additives is a significant step by the Agency in grappling with these problems.[25] In certain circumstances, the April, 1982, proposal permits FDA to use risk assessment and risk management techniques in making safety determinations. However, the proposal has limited application and challenges have been brought questioning FDA's authority to act in light of restrictive statutory language.

E. Packaging Presents Distinct Regulatory and Health Concerns

Separate statutory treatment for packaging and other food-contact substances is merited because the use and potential for ingestion of these substances differ dramatically from substances directly and deliberately added to food. Consequently, different regulatory approaches are needed. When substances are directly and intentionally added to food, there is little, if any, disagreement concerning their presence or the quantity involved. The only issue to be decided is whether the additive is safe. For packaging materials and other food-contact substances, however, the controlling question is often whether any of the material migrates into food and, if so, how much. If there is no detectable migration with an adequately sensitive test method, toxicological issues are essentially irrelevant.

FDA recognizes these differences. In 1982, the Agency issued a revised handbook for assessing the toxicological properties of direct food and color additives. To explain why the handbook did not apply to indirect additives, which are treated separately, FDA stated:

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[25] 47 Fed. Reg. 14,464 (Apr. 2, 1982).

> The safety review of indirect additives often involves different chemical structure classes, and special problems in estimating consumer exposure, including the possibility of migration of miniscule amounts of chemical substances to food that make them of extremely low or no toxicological concern in terms of food safety or for the purposes of applying legal standards. Therefore, FDA intends to publish a separate system of tiered information requirements for indirect additives.[26]

European health officials have also concluded that indirect additives require a different regulatory approach than direct additives. During a May 25, 1983 meeting, the Superior Council of Public Health of France, Food Hygiene and Nutrition Section, issued a proposed circular to govern food-packaging materials. The introduction to Appendix II of the proposed circular states:

> The circular of August 8, 1980 relative to applications for authorization for the use of substances intended to be intentionally introduced into foods (additives and technological auxiliaries) fixed an examination protocol which cannot justifiably be applied to materials in contact with foodstuffs when no significant contamination is to be feared under good manufacturing conditions.
>
> It is therefore necessary to establish a protocol which takes into account the degree of contamination of foods which can result from their contact with these materials.

Overall, the French system appears to be quite flexible and permits the free use of scientific judgment depending on the particular situation under review. But, we note the French proposal and FDA's own conclusion only to demonstrate that because the questions initially facing FDA are distinct, the realities of regulatory practice mandate separate treatment for indirect additives.

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[26] FDA, Toxicological Principles for the Safety Assessment of Direct Food Additives and Color Additives Used in Food, p. 5 (1982) (NTIS No. PB83-170696).

IV. CONCLUSION

The experience of the last 25 years teaches that industry significantly understated its fears of the impact of the 1958 Food Additives Amendment and that Congress also misjudged the adverse effects that would follow. There is a pressing need for a simplified approval procedure for food-contact substances apart from the existing rulemaking proceeding designed for direct food additives. At the present time, it can take three or more years between the filing of a food additive petition and final approval. Often this process takes even longer. Ultimately, FDA has been forced to misallocate or waste its administrative resources in the food area. Moreover, current law can be and is construed to bar substances even when the risk is insignificant.

These hearings are intended to investigate whether there is a need to amend the food safety laws. In our view, the obvious answer is yes. We urge the Committee to develop legislation as soon as possible. Part of this task will be aided by the Committee's staff working draft, dated April 20, 1983, and the recommendations of FDA and USDA contained in the Sub-Cabinet Council Working Group's draft language of September 3, 1982.

The efforts of both these groups, and legislation introduced in the last Congress by Senator Hatch as S. 1442, provided for a premarket notification system for indirect additives as an alternative when a full-blown food additive petition and rulemaking is not needed. Such a provision is long overdue. Other laudatory provisions directed FDA to issue regulations clarifying when a food-contact substance would be considered a food additive and what level of migration may be considered de minimis, as that term was used by the court of appeals in Monsanto Co. v. Kennedy.

Apart from provisions addressing food-contact substances specifically, we also urge that Congress clarify the definition of "safe" and permit FDA to use the best available scientific approach to making safety determinations. We agree with the FDA-USDA and Committee staff formulations that equate safety with a showing that potential risks are negligible. Similarly, the Delaney Clause should be modified, in light of the changes in analytical chemistry and the court's holding in Monsanto Co. v. Kennedy, to deal with trace amounts that pose no threat to the consumer.

Collectively, such amendments will improve the regulatory system, adapt it to changing scientific realities and continue to protect the public health. I appreciate this opportunity to present the views of the plastics industry and would be glad to answer any questions you might have.

(Note: In the interest of economy, the appendixes to Mr. Heckman's statement were retained in the files of the Committee where they may be researched upon request.)

The **Chairman**. Thank you, Mr. Heckman.

Our last witness will be Mr. Ritchie Jordan, who is testifying on behalf of the National Pork Producers Council.

Mr. Jordan, we will turn to you at this time.

STATEMENT OF RITCHIE JORDAN, LEGISLATIVE COMMITTEE MEMBER, THE NATIONAL PORK PRODUCERS COUNCIL, SUFFOLK, VA.

Mr. **Jordan**. Thank you, Senator Hatch.

I am Ritchie Jordan. I am a pork producer from Suffolk, Va.

We appreciate this opportunity to present our position on food safety and some recommendations which we urge the committee to consider.

The National Pork Producers Council has over 110,000 dues-paying, producer farm families as members. It is funded entirely by a voluntary checkoff program which collects two dimes per market hog at the marketplace. Producers who voluntarily participate number well over 200,000.

The goal of our relatively young organization is to improve the profitability of pork production. We provide consumers with information concerning the nutrition and the economic value of pork. We recognize that consumer confidence in the safety and wholesomeness of the food we produce is of paramount importance. For this reason, we have been actively involved in seeking changes in our current food safety law.

We have had firsthand experience with the application of the present law, an experience we cannot afford to have again from the mishandling of scientific data. There is no need to repeat the whole story of the Newberne report and nitrites. I understand that this has been done earlier in the week, and action taken by the FDA and the USDA was related.

During the 2 years that the cloud of carcinogenicity hovered over the cured meat products, especially bacon, the pork industry lost a billion dollars or more because of the depressing effect on the consumption of pork products.

Testing trials similar to the one conducted by Dr. Newberne are always in progress, and the results are frequently submitted to one of the Federal agencies. How these results are reviewed and evaluated is of utmost importance, not only to pork producers but to all other food producers, processors, and consumers.

We have been participating with other farm and agribusiness organizations in the development of revisions to our food safety laws. As a result of these deliberations and our continuing effort to review the issues, the NPPC had a position on food safety law changes for almost 2 years.

Since the present food additive amendments, including the Delaney clause, were enacted, there have been revolutionary, scientific, and technological changes. The ability to detect has outstripped our knowledge to interpret what we detect.

Some scientists maintain that certain chemicals are dangerous at any level, even down to the molecules. Even though this may be theoretically true, there is much more evidence that there are no effect levels and that just detection of some chemical does not mean that it presents a danger in our foods.

When the Delaney clause or amendment was adopted, the Secretary of what was then HHS testified that the Delaney clause was not arbitrary and unscientific, that the science was utilized in determining what was a carcinogen. Mr. Chairman, I maintain that this philosophy has changed along with the science. Too often now, any amount of a substance that does not kill the animal, if the so-called maximum tolerated dose can be shown to cause tumors, the substance or chemical is labeled a carcinogen.

There is increasing discussion that chemicals and substances that cause tumors can be classified as activators, promoters, modifiers, and that other substances cause hyperplasia because they are acutely toxic.

Other scientists, such as Dr. Robert Squire, propose a system for ranking animal carcinogens. All of this argues strongly for more flexibility and discretionary authority in handling the food safety question. This also supports a definition of safe that clearly eliminates the zero risk or zero tolerance attitude that prevails in the minds of some regulators and activists today.

We believe that no significant risk terminology as a definition of safe is preferable to the no harm. We also recognize the implications of the term significant from a statistical sample, and therefore recommended some other wording, such as negligible risk perhaps instead of no significant risk.

In any case, a definition of safe that clearly connotes that the zero risk concept is not intended by law will be an improvement.

Our previous discussion of the flexibility that must be available in administering the Delaney amendment is essential. Risk assessment must be permissible for not only substances that are possible carcinogens, but also for other additives. This principle is more important than just which risk will be considered as balanced against which benefit.

Provisions of the law should make it perfectly clear that Congress intends the administering agencies to make such assessments in decisionmaking. We strongly believe in peer review. We believe that there may be two levels of peer review. The first, we suggest, should be made before certain conclusions are reached—what is a carcinogen? With these kinds of first-call decisions, we believe agency personnel should have the benefit of outside peer review and consultation readily available. This review should be available in a manner less formal than an advisory committee.

There is no reason to believe that agency scientists and decisionmakers have all of the necessary knowledge to make these first-call decisions; that is, the Newberne nitrite study could have been properly categorized at an early stage and avoided the embarrassment to the Government and the tremendous losses to pork producers.

However, when final decisions are being made with regard to permissibility of an additive or withdrawal of substance from our food supply, we believe that there must be a formal peer review committee. We seriously question the value of a standing advisory committee of outside scientists. These standing advisory committees have been employed in both FDA and USDA over the years and have proven of no detectable value. Some are mandated by law and will, no doubt, have to be continued but should not be looked upon for any scientific assistance in resolving difficult food safety questions. The amount of time that such busy people can allocate to the question presented, their lack of experience with the regulatory procedures and organizations and the political pressure placed upon members of these committees does not make them useful for resolving truly scientific questions.

We recommend that there be established an interagency committee, council, or board, perhaps by the President, composed of one senior scientist from each agency. The agency should include at least the Food and Drug Administration, the USDA, the Environmental Protection Agency, the Occupational Safety and Health Administration, the Consumer Products Safety Commission, and the National Cancer Institute. There might be another agency or two that should be represented.

Each senior scientist should be given a small staff and have service on this interagency council as a sole responsibility.

We believe that there are well-qualified, experienced scientists at each agency who would welcome this opportunity.

With this type of interagency, governmentwide scientific board, we would go far toward establishing reasonable, practical, and enforceable regulations under any law. It would also provide for uniformity between Government agencies and regulations on substances in our water, food, and environment.

We believe that such a group of senior scientists from the agencies' career service should serve better than an advisory committee of outside scientists.

The Interagency Committee on Nitrites is an excellent example of how such a committee might work. If the nitrite carcinogenicity question had been referred to this group before a conclusion was drawn from the Newberne report, the whole nitrite debacle could have been avoided.

We also recommend that the final recommendations from the standing committee, if it is constituted as we have recommended, be binding on the agencies.

Mr. Chairman, that concludes my remarks. If there are any questions, I will be glad to try to respond to them.

[The prepared statement of Mr. Jordan follows:]

NATIONAL PORK PRODUCERS COUNCIL
P.O. BOX 10383, DES MOINES, IOWA 50306

STATEMENT TO THE
U.S. SENATE COMMITTEE ON LABOR & HUMAN RESOURCES
WASHINGTON, D.C.
WEDNESDAY, JUNE 8, 1983
BY
RITCHIE JORDAN

Mr. Chairman and Members of the Committee:

We appreciate this opportunity to present our position on food safety legislation and offer recommendations for Committee consideration.

The National Pork Producers Council (NPPC) has over 110,000 dues-paying, producer farm families in 38 member states. It is funded entirely by a voluntary checkoff program which collects two dimes per market hog at the market place. Producers who voluntarily participate number well over 200,000.

The goal of our relatively young organization is to improve the profitability of pork production. NPPC provides consumers with information concerning the nutrition and the economic value of pork and conducts research to improve the product for the consumer.

The majority of NPPC efforts in the information and promotion programs benefit consumers. We are constantly providing consumers with up-to-date information on the nutritional value of pork. Producers worked hard several years ago to have the studies undertaken to determine the nutritional composition of modern pork. I'm happy to report that those studies are being completed and will be generally available next fall. The Council works hard at dispelling the outdated views of pork and wants consumers to know that pork from modern hogs is a highly nutritious, healthful food that is a good buy in the supermarket. This leads me to our concern in regard to food safety legislation.

NPPC recognizes that consumer confidence in the safety and wholesomeness of the food we produce is of paramount importance. For this reason, we have been actively involved in accomplishing changes in our current food safety laws. Pork producers have had firsthand experience with the application of the present law - an experience we can't afford to have again from the mishandling of scientific data. There is no need to repeat the whole story of the Newberne report on the testing of nitrites for carcinogenicity or the hasty, unwarranted actions taken by FDA and the USDA. Suffice it to say that various studies by private organizations of the Newberne report which served as the basis for this cataclysmic announcement by the government agencies, revealed severe reservations about the report conclusions. Over the next two years, study after study of the Newberne report raised serious questions about its reliability as a basis for the announced need to discontinue the use of nitrites. Finally, on August 19, 1980, two years after the original announcement, the same agencies issued a statement, based upon a comprehensive study by pathologists and a governmental committee of scientists, "that insufficient evidence exists to support a conclusion that nitrite induced cancer in rats based on the MID (Newberne) study. As a result of the review and evaluation, we have concluded there is no basis for the FDA or USDA to initiate any action to remove nitrite from foods at this time."

During the two years that the cloud of carcinogenicity hovered over the cured meat products, especially bacon, the pork industry lost a billion or more dollars because of the depressing effect on the consumption of these pork products. It is impossible to determine accurately how much this unjustified cloud of carcinogenicity reduced the consumption of pork products. One estimate which is easily understood is that prior to the "cancer scare," pork bellies normally sold for between one and one-half and two times as much as live hogs. In other words, if hogs were bringing $40 per hundred weight "on the hoof," bellies would be selling for $60-$80 per hundred weight. For the two years while cured products were under suspicion because of the nitrite scare, they sold for the same price as live hogs, or sometimes less. During these years, 1978-1980, pork producers slaughtered over 80-million hogs a year.

It doesn't take a calculator or a Ph.D in economics to understand what a tremendous financial loss our industry suffered because of this improper handling of one scientific report. Testing trials similar to the one conducted by Dr. Newberne are always in progress and the results are frequently being submitted to one of the federal agencies. How these results are reviewed and evaluated is of utmost importance, not only to pork producers but to all other food producers and processors.

We have been participating with other farm and agri-business organizations in the development of revisions to our food safety laws. Although a "final" version has not been reviewed by our Council, we find that most of the thrust of drafts we have reviewed are consistent with our position on the changes needed in our food safety laws. NPPC has had an ad hoc committee on food safety legislation over a year. At one meeting, we met with representatives of the FDA, the Food Safety Council, the American Meat Institute, and with Congressman Wampler of Virginia and Congressman Martin of North Carolina. We also met with members of Congressman Foley's staff while he was chairman of the House Agriculture Committee. As a result of these deliberations and our continuing review of the issues, NPPC has had a position on food safety law changes for almost two years. The principle points of our policy are:

> The present body of food safety laws are outmoded, inflexible, inconsistent, and cause an erosion of consumer confidence in the safety of our food supply.
>
> The Delaney Clause of the Food, Drug and Cosmetic Act, and the Federal Meat and Poultry Inspection Act, need amending to include consideration of both health benefits and health risks in food safety policy.
>
> Current food safety laws embody a no-risk policy. This no-risk policy cannot accommodate our nation's latest technology that can detect the most minute traces of substances. Nor does it permit the type of regulatory flexibility necessary to address the complex scientific, economic and political questions that inevitably arise in these situations. A concept of acceptable risk, based upon scientific precepts is needed.

The following modifications to the food safety laws should be considered for the purpose of modernizing them and making them compatible with other existing health and safety laws.

1. The Food Safety Council, an independent organization of scientists, worked for several years to develop a procedure for evaluating the toxicity of substances. The NPPC believes this scientific review process should be utilized by the responsible regulatory agencies in making toxicity judgment.

2. A policy is needed to distinguish between food categories such as natural foods and added substances which will require different burdens for proof of safety for the different categories of food.

3. Policy is needed to preserve the concepts of GRAS (Generally Recognized as Safe) and prior sanctions provided in the present statutes.

4. The review and final determination of safety should be made by a body of senior scientists from the regulatory agencies operating as a special board and their conclusions should be binding on the agency concerned.

5. Authority for phase-out, or other flexible treatment of substances, should be defined for appropriate use.

6. Economic impact statements on all affected aspects of the industry should be required before final regulatory decision.

A careful review of our policy and the summary of the reports of the Working Group of the Administration reveals that most of these points have been reflected in these reports.

In the following, we will discuss in more detail, recommendations of the Working Group, how they are similar to or differ from our policy and what we recommend.

Although NPPC does not advocate the adoption of a definition of "safe," we recognize that this may be the best way to integrate an element of reasonableness in the administration or interpretation of our food safety laws. The definition suggested by the reports seems to dispel the idea of absolute safety or no risk. We believe this is important and an important first step in achieving more acceptable food safety decisions. Whether or not NPPC has the best definition of safe that can be written is not as important as to recognize that a definition of "safe" is necessary and certainly conforms to our statement of policy on the changes needed in the Delaney Clause and the present statutes.

In the same connection, we believe that the modifications to the Delaney Clause suggested in the reports are desirable and supportable. NPPC especially recognizes the desirability of the modifications pertaining to the so-called DES proviso. We have long known that the ability to detect has far exceeded our ability to interpret the significance of the minute amounts that can now be detected. Also, the recognition of the effect of the metabolism of chemical substances in the animal's body is an important acknowledgement that must be considered in the total evaluation of the presence of carcinogenic substances in animal feed. Another especially important part of the report pertaining to the Delaney Clause and the use of animal drugs is the "no residue -- presenting a significant risk to human health will be found." This phrase will be helpful to the agencies in implementing the Delaney Clause as it relates to animal drugs. The additional qualifications suggested as being pertinent in the evaluation of possibly carcinogenic substances are positive interpretations and should be included in any revision of the Delaney Clause.

NPPC notes with approval, too, the reference to "phase out" authority. The wording in H.R. 4014 and S. 1442 introduced in the last Congress is preferable to the suggestions of the reports from the Working Group in our opinion. How best to word this is not as important as to provide phase out authority.

We also endorse the realignment of food additive categories and the recognition of traditional foods. This also is in accord with our position on food safety law changes. NPPC was perturbed, however, by references in the reports as to how GRAS substances would be affected. We do not believe that use prior to 1958 "under the conditions of its intended use" is a valid criterion. It would seem to remove FDA and USDA's authority to make common sense judgments in regard to many substances.

We have the same concern in regard to the proposal regarding prior sanctioned substances. We believe that the burden of proof should reside with FDA in determining that a prior sanctioned substance "may be injurious" to health. NPPC, therefore, opposes these changes and refers to our third policy reference in regard to preserving the GRAS and prior sanctioned provisions of the present statutes.

We are pleased to observe the recognition of the need for scientific reviews by peer scientists on questions of food safety. We also endorse the incorporation of this requirement in the revised statutes. We cannot, however, concur in the proposed plans for the utilization of these scientific reviews. We do believe there can be merit in the utilization of scientists outside of the government as ad hoc advisors early in the scientific evaluation process. These provisions should be as informal as necessary to achieve what is really sought - qualified scientific advice on basic questions - to assist the regulatory scientists in arriving at a safety conclusion. This availability of well qualified scientists to the "working level" agency scientist will be useful and valuable in making scientific judgments which are obscure and require the greatest possible scientific competency. However, we want to emphasize that for scientific peer review to be useful, it must be readily available on an ad hoc basis. It must be under minimal administrative clearances or the "trouble" connected with the use of these outside scientists will discourage their use.

NPPC seriously questions the value of a standing advisory committee of outside scientists. Standing advisory committees employed by both FDA and USDA over the years have proven of no detectable value. Some committees which include non-scientific members are mandated by law and will no doubt be continued, but should not be looked to for any scientific assistance in resolving difficult food safety questions. The amount of time that such busy people can allocate to the question presented, their lack of experience with the regulatory procedure, and "political" pressures raises serious question about their ability to resolve truly scientific questions.

NPPC recommends that an interagency committee, council or board composed of one senior scientist from each agency be established. The agencies would include, at least, the Food and Drug Administration, the USDA, the Environmental Protection Agency, the Occupational Safety and Health Administration, the Consumer Product Safety Commission, and the National Cancer Institute. Each senior scientist should be given a small staff and devote his or her full attention to this interagency council. We believe there are well-qualified, experienced scientists in each agency who would welcome this opportunity. With this type of interagency, government-wide scientific board, we would take a major step toward establishing reasonable, practical and enforceable regulations under any law. It would also provide for uniformity between government agencies in regulating substances in our water, food and environment. NPPC believes that such a group of senior scientists from the agencies' career service could better constitute the "Standing Committee" referred to in the Working Group's report.

The Working Group on Nitrites is an excellent example of how such a committee might function. If the nitrite carcinogenicity question had been referred to this group before conclusions were drawn from the Newberne report, the whole nitrite debacle could have been averted.

We also suggest that the final recommendations of the "Standing Committee," if it is constituted as we have recommended, be binding on the agencies.

The specific provision which we recommend be included in legislation specifies that FDA and USDA utilize the procedures developed by the Food Safety Council in evaluating the safety of food substances.

We understand that some of the best qualified scientists in the U.S. worked for many months in developing the "decision-tree" approach. Although we are certain that the Committee and its staff are well aware of this study, we are referring to the Proposed System for Food Safety Assessment which is the final report of the Scientific Committee of the Food Safety Council. Although we are not in a position to endorse this entire report, we do recommend that this legislation or the legislative history and report accompanying this legislation, recognize this comprehensive study and that special reference be made to the Safety Decision Tree found on page 11 of this report as Figure 1 (copy attached).

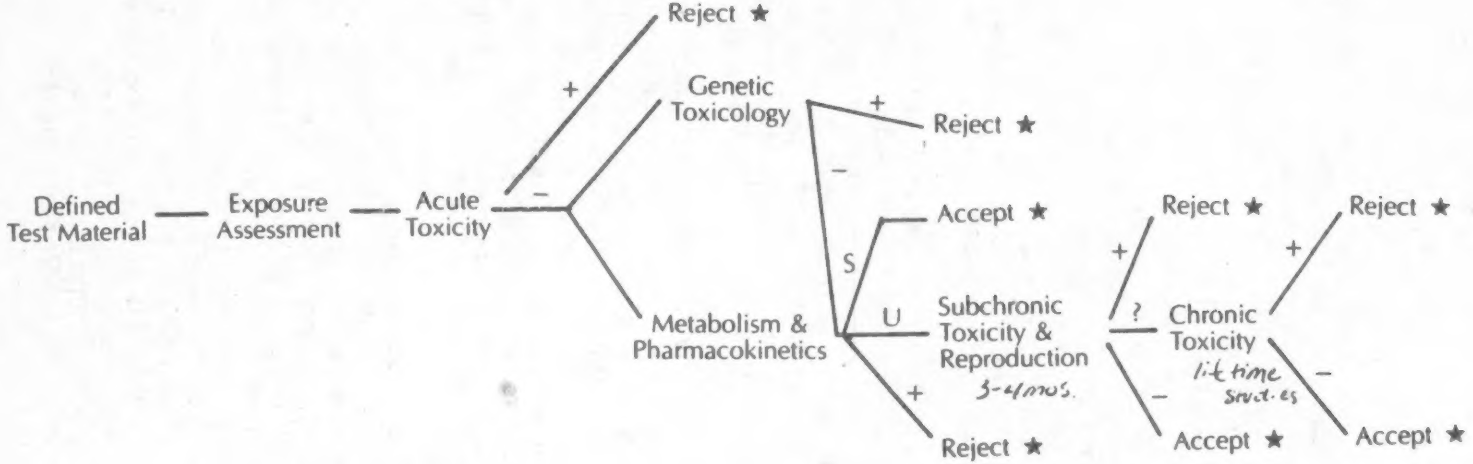
Mr. Chairman, this completes our testimony. Thank you for the opportunity to present our views on this vital issue.

Respectfully submitted,

Ritchie Jordan
NATIONAL PORK PRODUCERS COUNCIL

Figure 1

SAFETY DECISION TREE


Defined Test Material
Exposure Assessment
Acute Toxicity
+
Reject ★
−
Genetic Toxicology
+
Reject ★
−
Metabolism & Pharmacokinetics
S
Accept ★
U
Subchronic Toxicity & Reproduction
3-4 mos.
+
Reject ★
+
Reject ★
?
Chronic Toxicity
lit time studies
−
Accept ★
+
Reject ★
−
Accept ★

+ = presents socially unacceptable risk
− = does not present a socially unacceptable risk
S = metabolites known and safe
U = metabolites unknown or of doubtful safety
? = decision requires more evidence
★ = see Summary, page 5.

The CHAIRMAN. Thank you so much.

Let me just ask those of you who care to comment this: When Drs. Kennedy and Goyan testified on Wednesday, they mentioned several areas where they thought existing law needed change. I might add they have been followed by a wide range of scientific and other testimony basically agreeing with them. The panel previous to this one, however, has suggested that such changes will amount to weakening the present law.

Your industry—or your industries, I guess I should say—have a great stake in maintaining a safe food supply.

How would you respond to the previous panel's testimony?

Mr. GARDNER. Maybe I could take a first crack at that, Senator.

The CHAIRMAN. Sure.

Mr. GARDNER. First, I think Dr. Roberts earlier put his finger on one important aspect, and that is priority of attention. It is essential that some change be made so that the agencies can divert or direct their resources to those things that are really important and neglect the things that are less important.

Another factor to consider is that every time the agencies direct their attention to things that are trivial and silly, they simply bring regulation into further disrepute, disregard, and destroy any credibility it has with the American people. That, we would regard, as a lack of protection.

Third, several people here have mentioned the fact that the industry does have a great stake in maintaining the safety of the food supply. Let me assure you that the members of our industry have a great deal invested in their product. They all sell brand-name merchandise. I suggest to you that this investment in reputation and name people are not willing to sacrifice readily or put at risk. They are not likely to want to do anything that would bring the safety of the food supply into disrepute.

The CHAIRMAN. Would anyone else like to comment?

Mr. HECKMAN. I think we probably represent a unique situation where a lot can be achieved without the remedy being so apparent or even so antithetical to the desires of the consumer groups.

The packaging industry regulations are virtually unbelievable. If you could just take a look at them, I think you would see what I mean. They occupy about two-thirds of the Code of Federal Regulations pages devoted to food additives regulations. I confess to being responsible for many of those, but I did not have a lot of choice.

The problem there is that they are beating something to death that can be handled a lot more simply, and not only more simply, but there is a way to do the job that would give the public and the packaging industry's customers represented here at the table more assurance that the products they are buying are safe.

The current system puts a lot of stress and emphasis on generic regulation treatment, and therefore puts Food and Drug in the position of having to adopt standards that are not really that enforceable because they have to deal with a situation generically that is better dealt with in most cases at least on a specific case-by-case basis. This is an area for simplification and savings where the improvements may not seem dramatic but would be.

Again, if you remember, the Assistant Director of the Bureau of Foods says that they spend 85 percent of their time on indirect food additive regulations. If that could be cut in half, then 40 percent of the FDA staff time could be devoted to the kind of issues that I believe former Commissioner Gardner was speaking about.

The **Chairman**. Thank you.

Dr. Roberts?

Dr. **Roberts**. I would just like to reiterate what Mr. Gardner said but in perhaps a different way.

Mr. Chairman, you asked the prior panel what would happen if the law were not changed, and I think that is another important way of looking at the food safety issue.

As Dr. Hayes and Mr. McMillan pointed out this morning, without the kinds of changes in the law that we have been talking about, there will clearly continue to be a sense of frustration on the part of the regulator. There are all the problems with implementing the law that the various Commissioners spoke of.

I think we have to clearly recognize that those problems are not going to go away. They are going to increase as the scientific advances continue that we have had in the past 25 years.

What that brings us to, then, clearly is the necessity, without changes in law, for the Congress to deal with these problems on a case-by-case basis. I do not think that is the optimum way for the Congress to operate in protecting the public health.

The **Chairman**. I can sure testify to that because of the saccharin issue alone. We have spent a lot of time just trying to overcome what we thought was somewhat of a ridiculous posture and approach that was taken. Congress, as you know, has had to do it on a regular basis. There is no doubt, if they can conclusively prove that it is carcinogenic to human beings in the fullest sense or a significant risk to human beings, we probably will not continue to do that. However, they have not made that case, and we all know it and they know it.

Dr. **Roberts**. That is true, very true.

I think another point on the list I made during the presentation of the last panel is this: I think we have to look at the point that a number of us have brought up, and that is the stifling of innovation. In the scientific panel, Dr. LaBuza pointed out what I think are some very exciting possibilities for new food products and food product packaging. Especially in the areas of generic engineering, there are marvelous opportunities for us all to take advantage of, and which would accrue to the public benefit.

However, as Dr. LaBuza pointed out, under the current law there is little incentive to pursue those kinds of things. Indeed, they would be difficult to bring on the market.

As we have said in our earlier discussion, Mr. Chairman, the net effect if the law is not changed and if therefore we cannot focus on priority problems, as Mr. Gardner just said, is that the public protection suffers. I think this clearly points out that we do, in fact, need changes in the law.

The **Chairman**. Mr. Jordan.

Mr. **Jordan**. Senator Hatch, I feel that the pork producers support the changes that have been proposed: the redefinition of "safe," and the phaseout.

We feel that the greatest problem in the handling of the nitrite was that the peer review process broke down. To determine what is scientific fact, we feel that there should be a uniform approach to it, so that we do not have differences in the way that it is done from agency to agency and from administration to administration. That, to us, was a real crucial problem, in the *nitrite* case and we feel we were penalized unnecessarily.

The CHAIRMAN. I would be interested in further discussion on this area. If any of you care to submit any written answers to this question, I would appreciate that as well.

Let me bring this to a close.

I think that these have been extraordinary and historic hearings held over the last 3 days. We have had eight panels of witnesses, including former Commissioners of the Food and Drug Administration, top health officials in Government, and top scientists in the country. Of course, much was said, and there was a lot of consensus on the need for change by those who are the top thinkers in this field.

There has been some disagreement, as you know, primarily by the one panel.

I believe that these hearings have been an important step toward rationally addressing the issues that you have felt are so important, and I have to confess I feel are extremely important.

I think that it is a commendation to the heat on this issue—and I might add to the interest in this issue—that here we are at 1:15 on a Friday, 4 hours after we started, and we still have people standing in this hearing room. There is a lot of interest in this particular issue. We have had a full hearing room throughout and really a jampacked one for most of the hearing today.

I might also say that we have spent tremendous effort on this committee, and I might say we have a tremendous investment of this committee, in hearing all of the views. We have tried to bring the best people we can in on all sides of this issue, and I believe we have succeeded in doing that, as hopefully we do on all issues.

I just want to personally thank all of the witnesses for coming and thank all of you for being here today. All who have participated have been very helpful to this committee.

I should hope not, we might be able to resolve these problems after 25 years of not benign, but I think, in some ways, willful neglect because it is a tough political issue with which to deal. I hope we can resolve them in the best interest of the health and safety of all people in our society. To that extent, I think every witness has tried to testify to his or her best ability to try to help our society to have better health, better safety, better food, and better food products and packaging.

I really appreciate everybody who has testified. We will now have to take some time and assimilate these materials, look at them, and make some final conclusions. I personally believe that we are going to have to come up with some legislation—and Congress is going to have to do what it really should do, and face these tough problems in the best interest of everybody in America.

I understand that Senator Grassley may be submitting questions for the various panelists.

[Questions and additional statements and material supplied for the record follow:]

ADDITIONAL QUESTIONS FOR INDUSTRY PANEL PREPARED BY SENATOR HATCH

Question: During the hearing several witnesses discussed the effect of current law on innovation. In your opinion, does current law stifle innovation? How? Please provide examples to support your conclusion.

Answer: (Dr. Roberts): Current law undeniably stifles innovation of new products in several ways. First, the rigidity of current law, particularly the Delaney Clause and the drift toward a zero risk policy, is a significant disincentive to new product research and development. Given the absolute prohibition of the Delaney Clause, a new and desirable additive, no matter how attractive its effects and no matter how trivial or negligible its risks, could not be permitted to be used if it were shown to induce cancer in laboratory animals. A company considering investing in research on new additives or food technologies is unlikely to make that investment if it has any reason to believe that the additive may turn out (or is already known) to induce cancer in laboratory animals, even if the company believed that it could establish persuasively that the risks of the additive under its intended conditions of human use were negligible or even nonexistent. The inflexibility of current law and the relative ease with which a new product can get derailed by a single adverse study in laboratory animals, clearly makes many companies unwilling to engage in the extremely costly and time-consuming process of research, development and application for regulatory approval.

The experience of the Monsanto Company with its acrylonitrile copolymer bottle illustrates the effect on innovation of an overly restrictive law and regulatory policy which does not distinguish between risks to human health which are significant and those which are not. In that case, Monsanto expended a considerable amount of money to develop acrylonitrile beverage bottles and received FDA permission to market them. Thereafter, the agency, without sufficient regard to the risk, if any, from the bottles, withdrew its approval. And, although a court subsequently ruled that FDA had discretion not to treat as a food additive low level migrants (indirect additives) which presented no public health concerns (Monsanto v. Kennedy), Monsanto had by then lost a significant amount of money and the market for its bottles. An experience such as that unquestionably makes many companies cautious about investing in new products and technologies.

The Delaney Clause adversely impacts on desirable innovation in at least one additional way as well. The clause leaves no room for scientifically sound judgments about risk, but rather assumes that all substances shown to induce cancer in animal studies present unacceptable risks to humans under actual conditions of use. Therefore, a single study in animals suggesting that an additive might be an animal carcinogen, notwithstanding substantial evidence that the substance does not present significant risks, may well delay substantially, and possibly derail altogether, the use of a safe and desirable additive or technology.

In his testimony before this Committee, former FDA Commissioner Goyan recounted an example of the delay caused by excess regulatory concern over trivial risks, concern which is a function of the Delaney Clause. Unnecessary delay is a serious impediment to innovation.

"Brikpak" is an aseptic packaging innovation, which permits paper board food containers to be sterilized so that refrigeration becomes unnecessary. Although it is clearly an important, useful, and desirable packaging innovation, it took FDA three years to authorize its use, because as Dr. Goyan stated, FDA was hung up on the use of hydrogen peroxide to sterilize the product, which, apparently, was associated with cancer in one animal study. As Dr. Goyan noted, the delay in resolving this concern occurred even though FDA scientists acknowledged that they were not concerned about any risk to humans and recognized the desirability of the packaging innovation.

FDA delays in product approval have inhibited innovation in a number of other areas such as in the development of retortable containers -- plastic laminated containers that can be hermetically sealed and can thus be used like metal cans to store food without refrigeration.

In each instance, delay and uncertainty caused by an inflexiblelaw discouraged U.S. Companies from developing and marketing new food products and food product packaging.

The absence of a definition of "safe" in current law also inhibits innovation. Because the law does not now define "safe," FDA policy in recent years has drifted toward a "zero risk" approach. This drift, the uncertainty and unpredictability that it causes, and the "moving target" that it presents, makes it difficult for companies to justify the investment in product and packaging innovation. Likewise, the excessive strictness of a "zero risk" policy increases the likelihood that an additive or technology will be prohibited, even if the proponent of its use can demonstrate that the risks are insignificant. By not focusing regulatory attention on whether risks are significant or not, marginal issues and trivial concerns can deprive companies and the public of desirable innovation, or significantly delay its introduction. Delay, of course, is not without its costs, for it deprives companies of valuable patent time, permits competitors to "catch up" and thereby diminishes the financial reward that the investment of the innovator warrants.

Earlier in this hearing Dr. Theodore Labuza cited the areas of irradiation and special purpose preservatives as other examples of the stifling impact of current law on innovation. Such examples are quite useful in illustrating existing reasons for modernizing food safety law. In addition, the examples mentioned by Dr. Labuza of future adverse impacts on innovation are equally illustrative and worthy of being repeated. These latter examples include special foods for weight control and reduction, medical foods, "mood foods," and the products of genetics engineering and other applications of biotechnology. In the absence of modernization of food safety law the extensive benefits that could accrue to mankind from these advances could be significantly curtailed.

2) Saccharin was mentioned frequently during the hearings. Please describe for the record research on saccharin conducted since 1977 when FDA proposed the ban.

Since the FDA's proposed ban of saccharin in 1977 there has been a great deal of research, the results of which strongly support the safety of saccharin for human consumption. The saccharin studies conducted since 1977 can be discussed in two categories, epidemiology (human use) studies and laboratory (primarily animal) studies.

Epidemiology Studies

A variety of saccharin epidemiology studies of different types and pertaining to different countries have been conducted over the years. Although proving an absolute negative obviously is impossible, the collective epidemiological evidence on the lack of hazard of saccharin for human consumption is overwhelming. Such extensive evidence of safety has not been accumulated for any other food ingredient.

In all, there are about twenty epidemiology studies supporting the safety of saccharin at human levels of consumption. Significantly, the most important of these studies have been completed since 1977. Foremost among recent epidemiology studies is the study sponsored in part by FDA and conducted by the National Cancer Institute (NCI). The NCI study, involving about 9,000 subjects in ten areas throughout the country, looked at the consumption of artificial sweeteners (saccharin and cyclamate) relative to the incidence of human bladder cancer.

The NCI Study was reported on in December 1979 (1) and in part concluded, "In the total study group, there was no evidence of increased risk with long-term use of AS (artificial sweeteners) in any form or with use that began decades ago." Furthermore, the study report indicated that even individuals consuming the most saccharin and for the longest periods of time had no increased risk over individuals not using saccharin at all. There were sub-groups of subjects in the study that had so-called "relative risk ratios" greater than one (which mathematically would indicate an increased risk). However, there were also sub-groups with relative risk ratios less than one (which mathematically would indicate a decreased risk). In most cases these risk ratios involve too few subjects to be statistically significant and cannot be interpreted as showing either increased risks or protective effects (2).

In 1982, an independent review of the NCI study data, conducted by Epidemiology Resources, Inc. (ERI), was published (3). This review was undertaken in order to provide an independent analysis of the NCI data by expert epidemiologists. The ERI review confirmed the NCI findings and specifically concluded: In the general study group, there was no evidence for an association between non-nutritive sweeteners (saccharin and cyclamate) and bladder cancer.

The review team also addressed the data for sub-groups in the NCI study and concluded ". . . that the data provided little evidence that non-nutritive sweeteners increase the risk for bladder cancer among subgroups of users."

Among other recent epidemiology studies, Morrison (4), in 1979, found that ". . . an age-sex-country-standardized estimate of cancer incidence showed no increased risk" for artificial sweetener users based on over 12,000 subjects in seven countries. In 1980, Morrison and Buring (5) concluded from a study of over 1000 subjects that, ". . . as a group users of artifical sweeteners have little or no excess risk of cancer of the lower urinary tract." The authors also noted that, "Increasing frequency or duration of exposure was not associated consistently with an increasing relative risk."

A study of over 1,000 subjects reported by Kessler and Clark (6) in 1978 concluded that, ". . . neither saccharin nor cyclamate is likely to be carcinogenic in man, at least at the moderate dietary ingestion levels reported by the patient sample."

In 1980, Wynder and Stellman (7) reported on a case-control study of artifical sweetener use and bladder cancer involving 302 male and 65 female bladder cancer patients and an equal number of matched controls. The authors concluded:

> . . . no association was found between use of artificial sweeteners or diet beverages and bladder cancer. No dose-response was observed with respect to quantity or duration of use or the two combined. No evidence was found to suggest that artifical sweeteners or diet beverages promote the tumorigenic effect of tobacco smcking.

Epidemiological investigation of human in utero exposure to saccharin was investigated by Jensen and Kamby (8) of the Danish Cancer Registry and reported in 1982. Evaluation of human in utero exposure is important because of animal experiments showing effects only at high doses when the fetus is exposed from the mother's food. The authors noted that:

> In Denmark the use of saccharine [sic] increased sharply during the second World War as a result of scarcity of sugar and import and export figures indicate that saccharine [sic] consumption was on average 4-5 times higher during the war-time period than in the pre-war decade.

The authors concluded in summary, This study provides no evidence of an increased risk of human bladder cancer during the first 30-35 years of life associated with in utero saccharine [sic] exposure.

In a somewhat related study reported by Morrison, et al. (9), the relation between artificial sweeteners and bladder cancer was evaluated in Manchester, U.K. and Nagoya, Japan, areas where extensive use occurred 30-40 years ago. The authors concluded, "A history of use of sugar substitutes primarily saccharin, was not associated with an elevated risk of bladder cancer in either study area." Data on dietetic beverage use was not obtained in Nagoya but was for the Manchester study, which led to the conclusion that, "This exposure was not associated with a greater risk of bladder cancer." Overall, the researchers concluded, "The results of this study suggest that use of artifical sweeteners confers little or no risk of bladder cancer."

As previously noted, the epidemiological evidence supporting the safety of saccharin is now overwhelming, with much of that evidence originating since the proposed ban of saccharin in 1977. That evidence is most reassuring since it pertains directly to human use. Nonetheless, under current food law, regulatory decisions must be based on existing animal research and that area is also of interest.

Animal and Other Laboratory Studies

As is the case with epidemiology, significant laboratory research has also been conducted since 1977. The most significant such research is described in the following, after first noting some brief background information.

Based on the Delaney Clause concept of an animal "carcinogen," that is, a substance associated with an increased incidence of tumors in animals, regardless of the test conditions, saccharin in general would be classified as an animal "carcinogen," albeit a weak one with an associated risk (if any) probably no greater than that equivalent to the risk of death from lightning (2). However, it is becoming increasingly apparent that such a simplistic definition as that posed by the Delaney Clause does not even begin to provide an adequate characterization of saccharin.

It has been established (10) that saccharin is not metabolized in either man or rat, does not bind to DNA in rat liver or bladder, nor does it produce other cellular effects considered to be part of carcinogenesis. Saccharin does not accumulate in body tissues and is excreted unchanged in urine and feces. For the most part, saccharin does not show effects in the Ames test or in tests of mutagenicity. Chromosomal effects occur with some inconsistency at very high doses corresponding to those showing increased tumor incidence in second generation male rats exposed in utero. As has been described by Cranmer (11), chronic tests performed prior to 1977 in several animal species including the mouse, hamster and primates, and in several single generation rat studies have not shown increased bladder cancer incidence or other carcinogenic effects.

Saccharin is a relatively inert substance and, ironically, is in fact so innocuous that it can be fed at the abnormally high levels required to produce effects in the second generation male rat. If saccharin were more like most other test substances, it could not be fed (because of acute toxicity) at such high levels and no effects would have been evidenced (2).

By far the most significant animal research performed with saccharin since 1977 is the large-scale rat study conducted at the International Research and Development Corporation (IRDC) and reported in May, 1983 (12). The IRDC study basically had two general objectives:

1) to determine the dose response curve in the high dose range; and

2) to examine as many as possible of the physiological changes associated with tumors.

The IRDC study utilized the most sensitive animal specie -- the Charles River CD rat; the most sensitive sex -- the male; and the most sensitive exposure period -- the second generation. Approximately 2,500 animals were involved, with a control group and six saccharin dose levels ranging from 1% to 7.5% of the rat diet.

An expert panel of international scientists under the chairmanship of Dr. Leon Golberg of Duke University Medical Center, reviewed the results of the IRDC study in the context of relevant published and unpublished research from previous studies and produced a summary report on the current status of saccharin (10). In part, the expert panel noted that:

> The results of the IRDC study, by better defining the dose-reponse relationship for bladder tumor risk in the rat, support the cónclusion that the present level of exposure of humans to saccharin through its use as a food additive is unlikely to present a cancer risk."

The panel also noted that at high doses in the rat, saccharin produced profound biochemical and physiological changes which do not occur in humans under normal patterns of use.

Dose response results from the IRDC study did not show a statistically significant increase in tumors at the 3% dose level for either benign tumors alone or malignant tumors alone, but the combined benign and malignant tumors were statistically significant compared to concurrent controls. In relative terms, a 3% level in the rat diet would correspond to human consumption of approximately 750 cans of diet soda daily. The IRDC researchers considered the 1% dose level (equivalent to 250 cans of diet soda daily) a no effect level.

Based on the IRDC study results, it appears that the effect of saccharin on the Charles River CD rat is indeed a unique high dose phenomenon. In addition, it appears that the observed tumor occurrence is associated with physiological changes which do not occur with normal human patterns of use. However, the exact mechanism or mechanisms involved in tumor production in the rat are not yet known and will require further research.

In making their evaluation of the current status of saccharin, the expert panel made use of information compiled by several investigators and consultants, including the following:

Ralph Riggin, Ph.D. - Characterization of Impurities in Commercial Lots of Sherwin-Williams Saccharin

Andrew G. Renwick, Ph.D. - The Metabolism and Pharmacokinetics of Saccharin in Rat and in Man

Robert Anderson, Ph.D. - The Effect of Ingested Sodium Saccharin on Nutrient Digestion and Intestinal Physiology

Andrew G. Renwick, Ph.D. - Effects of Saccharin on Tryptophan Metabolism

Steven D. Aust, Ph.D. - Role of Diet or Nutrition in Carcinogenesis

Bernard L. Oser, Ph.D. - A Review of the Saccharin Toxicology

Gerald P. Schoenig, Ph.D. and
Frank W. Carlborg, Ph.D. - IRDC Study Design

Edwin I. Goldenthal, Ph.D. - IRDC Organization and Study Implementation

Gerald P. Schoenig, Ph.D. - IRDC Study Quality Assurance and In-Life Results

Robert Anderson, Ph.D. - Bladder Divalent Cation Increase Caused by Saccharin Ingestion

Andrew G. Renwick, Ph.D. - Distension of the Urinary Bladder in Rats Fed Saccharin Containing Diet

Ward A. Richter, D.V.M., Robert G. Geil, D.V.M., and Charles H. Frith, D.V.M., Ph.D. - IRDC Study Pathology

Frank W. Carlborg, Ph.D. - IRDC Study Statistical Considerations

Morris F. Cranmer, Jr., Ph.D. - Biological Perspectives on the IRDC Study

John Ashby, B.Sc., Ph.D. - Genotoxicity on Saccharin: Relevance to Bladder Cancer

Samuel M. Cohen, M.D., Ph.D. - Multistage Carcinogenesis in Urinary Bladder

Robert W. Morgan, M.D. - A Review of Epidemiologic Studies of Artificial Sweeteners and Bladder Cancer

Philippe Shubik, D.M., D. Phil. - Saccharin: An Overview

The preceding papers, all contained in reference 12, constitute a comprehensive review of the current state of knowledge about saccharin and provide more detail about the IRDC study. Collectively they provide substantial support for the safety of saccharin for human consumption.

Conclusion

Since the proposed ban of saccharin by FDA in 1977, highly significantly research results have become available on saccharin. A variety of epidemiology studies, including one of the largest of its kind ever conducted (the NCI study) have consistently shown a lack of association between bladder cancer and human consumption of saccharin. The epidemilogical evidence of a lack of hazard from normal patterns of saccharin human use is overwhelming.

In the area of laboratory studies, the IRDC rat study is the most significant research completed since 1977. That study indicates effects in the rat only at dose levels equivalent in human terms to 750 cans of diet soda or more daily for a lifetime. More significantly, the IRDC study at those dose levels indicates profound physiological changes in the rat which do not occur in humans under normal patterns of use. The precise connection between those changes and the tumors occurring at high dose levels in the rat remains a question for further research. However, neither the extensive animal data nor the extensive epidemiological evidence indicates a hazard from normal patterns of human saccharin use. Saccharin is thus an important example of the need to modernize food safety law so that regulatory decisions can be based on the best science available.

REFERENCES

1. National Cancer Institute, Progress Report to the Food and Drug Administration From the National Cancer Institute Concerning the National Bladder Cancer Study, Washington, D.C. (1979).

2. Roberts, H.R., "Saccharin - Boon or Ban," Quarterly Bulletin of the Association of Food and Drug Officials, Vol. 45, No. 1, 1981.

3. Walker, A.M., Dreyer, N.A., Friedlander, E., Loughlin, J., Rothman, K.J., and Kohn, H.I., "An Independent Analysis of the National Cancer Institute Study on Non-Nutritive Sweeteners and Bladder Cancer," American Journal of Public Health, Vol. 72, No. 4, 1982.

4. Morrison, A.S., "Use of Artificial Sweeteners by Cancer Patients," Journal of the National Cancer Institute, Vol. 62, No. 6, June 1979.

5. Morrison, A.S. and Buring, J.E., "Artificial Sweeteners and Cancer of the Lower Urinary Tract," The New England Journal of Medicine, Vol. 302, No. 10, March 1980.

6. Kessler, I.I. and Clark, J.P., "Saccharin, Cyclamate, and Human Bladder Cancer - No Evidence of an Association," Journal of the American Medical Association, Vol. 240, No. 4, July 1978.

7. Wynder, E.L. and Stellman, S.D., "Artifical Sweetener Use and Bladder Cancer: A Case-Control Study," Science, Vol. 207, March 1980.

8. Jensen, O.M. and Kamby, C., "Intra-Uterine Exposure to Saccharine and Risk of Bladder Cancer in Man," International Journal of Cancer, Vol. 29, 1982.

9. Morrison, A.S., Verhoek, W.G., Leck, I., Aoki, K., Ohno, Y., and Obata, K., "Artificial Sweeteners and Bladder Cancer in Manchester, U.K. and Nagoya, Japan," British Journal of Cancer, Vol. 45, 1982.

10. Golberg, L., Cole, P., Conning, D.M., Mendelsohn, M., Mohr, R., Roe, F., Van Ryzin, J. Takayama, S., Truhaut, R., and Wagner, B., Saccharin - Current Status, Report of an Expert Panel, A report prepared for the Calorie Control Council, Atlanta, Ga., May 9, 1983.

11. Scherr, G.H., Editor, Saccharin, A Report By Dr. Morris F. Cranmer, Pathotox, Park Forest South, Ill. (1980).

12. Saccharin: An Update, A collection of papers compiled for the Scientific Review Panel on Saccharin, Calorie Control Council, Atlanta, Ga., May, 1983.

Question: In the National Soft Drink Association's comments on the Second Working Draft, you suggested that consideration of "health benefits" was too limited a criteria. How do you feel at this time about the scope of benefits which should be considered?

Answer: Many proposals to modernize current food safety law have included proposals for the consideration of "benefits." It is important to distinguish between health-related benefits of an additive, such as preservation or use for dietary management, and the economic effects of a prohibition on the use of an additive, such as the costs of alternative techniques to achieve a comparable effect in the food (e.g., freezing as a substitute for a substance that preserves food).

Before prohibiting an additive for which there is no practical substitute and which has a substantial history of use, FDA should be authorized to consider the effects on the public health of prohibiting or limiting the use of the additive, as well as the risks to health presented by continued use. Without such authority, FDA could be forced to ban a substance from food even if it acknowledged that the net effect of that action would be detrimental to the public health. In this context, "health benefits" should be broadly construed, but the decision criteria should not extend to economic effects.

In another context, however, that is when FDA and USDA have decided to prohibit the use of a substance, the law should permit the agencies to provide for the gradual elimination or phase-out of the substance. In considering how to implement a decision to ban, the agencies should be authorized to consider not only the consequences of the decision from the standpoint of the public health, but the effects on the cost and availability of food, and to structure a phase out which minimizes the adverse economic impact of the decision without exposing the public to unreasonable risks.

Question: Does your organization support the Administration's proposed definition of "safe," or do you feel that the Administration's definition could be interpreted as "zero-risk"?

Answer: The National Soft Drink Association prefers a straightforward "one-step" definition of "safe" which clarifies that an impossible "zero-risk" or "absolute safety" standard is not imposed under the Federal Food, Drug and Cosmetic Act. Such a definition was included in S. 1442, the Administration Working Group's first draft, and in H.R. 5491. These one-step definitions are clear and, unlike the Administration's Second Working Group draft, avoid resort to the phrase "no harm," currently found in the legislative history of the 1958 Food Additives Amendment, and the source of much current confusion in regulatory policy.

The National Soft Drink Association could, however, also support a "two-step" definition, such as that contained in the Working Group's second draft, although we believe that there is potential under that proposal for confusion about whether it perpetuates a "zero-risk" policy because it retains the "no harm" language. If a two-step definition embodying the "no harm" language is used, it should be accompanied by clear legislative history stating the intent of the Congress that the definition does not impose a requirement for proof of absolute safety. Likewise, the legislative history should not state or imply that the new definition makes no change in current policy, which has increasingly been interpreted as a "zero-risk" standard. Defining "safe" as, for example, "a reasonably certainty that the risks of a substance under its intended conditions of use are insignificant" states clearly an appropriate standard for regulating substances added to food. It should be noted that such a definition will not make the food supply less safe, but will ensure that substances are not prohibited because of inconsequential or trivial risks. The legislative history should clearly state this policy, regardless of whether a one or two-step definition is adopted.

Questions prepared by Senator Grassley

QUESTIONS FOR MR. JORDAN

NATIONAL PORK PRODUCERS COUNCIL

Question: In your comments on the Second Draft of the Administration's Working Group Recommendations, you found fault with the definition of "safe." Do you continue to feel that the Administration's definition of "safe" may mean "zero risk"?

Answer: Yes, we do. We prefer the definition in the first draft.

Question: Under a health benefits test, do you see the possibility of nitrite being banned since consumers could always eat fresh pork rather than processed pork products?

Answer: No, we believe that the food consumption patterns are so well established that there could never be a substitution for processed products. We believe that some alternative to nitrite would be found to be necessary even though the health benefits test was used.

STATEMENT OF CONGRESSMAN DON RITTER, 15th DISTRICT, PA
SUBMITTED TO THE SENATE COMMITTEE ON LABOR AND HUMAN RESOURCES
JUNE 9, 1983

Mr. Chairman,

It is an honor to submit testimony on the subject of food safety legislation before the Senate Committee on Labor and Human Resources. I would like to commend the Chairman for holding these hearings and thank him for the opportunity to share my views.

I strongly support the need to change the definition of "safe" in food safety legislation from one based on zero tolerance to one based on insignificant risk, as recommended in the original version of S.1442 in the 97th Congress. In conjunction, I strongly support the broad use of risk assessment in analyzing food hazards as a scientific means of designating which substances present significant risks versus which present insignificant risks. My position is based on the need to update food safety legislation to reflect the new knowledge gained and new techniques developed in today's world.

Food safety legislation has a long history beginning at the turn of the century with the Food Safety Law of 1906. This was followed in 1938 by the Food, Drug, and Cosmetic Act, followed in 1958 by the Food Additives Amendment which included the Delaney clause. These statutes were written with state-of-the-art knowledge available at that time. But knowledge has since increased and measurement techniques improved.

"Safe" is defined in the legislative history of the Food Additives Amendment of 1958 as a "reasonable certainty of no harm under intended conditions of use". In many cases, the Food and Drug Administration (FDA) has focused on the reference to "no harm" in its interpretation of "safe" to mean zero risk for all food substances. This interpretation came about partially because of the Delaney clause which applies a no-risk standard in its anti-cancer policy.

The Delaney clause prohibits the FDA from approving food additives, color additives, and new animal drugs that induce cancer in man or animals. The law is inflexible in that it does not permit evaluation of exposure, relative carcinogenic potencies, or the meaning of extremely small doses. My point is that while there has been an active interest in food legislation in the United States for almost 80 years, the improvement of chemical instrumentation technology and its ability to discern exceedingly small amounts means that some statutes on the books are out-dated today.

This was evidenced in 1977 under the Carter Administration when the Food and Drug Administration (FDA) tried to ban saccharin under the Delaney clause because there were test data which indicated that it caused cancer. Strictly speaking, under the letter of the law, saccharin should have been banned. However, after an evaluation of safety concerns, saccharin was not removed from the shelves.

This example exemplifies the inadequacies of the current laws to adapt to the current situation and demonstrates that even now FDA must judge the consequences of its administrative actions to the public. The reason saccharin is still available is well-documented and the judgement was based on a comparison of risks.

An artificial sweetener was deemed necessary, and there was not a known available substitute. Cyclamate, which is also an artificial sweetener, was a potential substitute, but had already been banned because at the time it was banned there was a known available substitute: saccharin. The irony in this case points out the subjectivity of the laws in the current system. If the saccharin data had been obtained first, cyclamates, which may actually be safer than saccharin, could be on the shelves today because there would have been no known substitute for a needed food substance (saccharin would already have been banned). There are numerous other examples of substances which should have been banned under the antiquated Delaney clause which are still available because of extenuating circumstances. Indeed, substances which recently have been indicted as carcinogens and would have been banned under a strictly-applied Delaney provision include oil of mustard and butylated hydroxyanisole (BHA).

Congress is aware of these discrepancies caused by laws which were formulated many years ago. Since 1981 efforts have been under way to revise the food safety statutes. The only problem has been that a consensus on how to revise these statutes has not yet been achieved.

These statutes need to be revised to more accurately reflect concern for food safety in a world of evolving scientific knowledge, a world which now includes sophisticated measurement techniques which were not in existence when these statutes were written, and sometimes-conflicting data regarding whether a substance is an animal or human carcinogen.

Measurement techniques are now so sensitive that they can detect parts per billion and even parts per trillion. Soon, if not today, these techniques will be able to detect individual molecules, and there is at least one individual molecule of a harmful substance in almost everything. This new technology further complicates implementation of the old statutes based on zero tolerance, because the detectable levels are dependent on the analytical capabilities, the testing methodologies, etc. The lower the levels of detection get, the more harmful substances are discovered in foods which had previously been deemed safe.

Sensitivities of measurement coupled with the Delaney clause requiring zero tolerance, mean that our food supply legally designated as "safe" is dwindling to almost nothing. So "eat, drink, and be merry" because tomorrow there may be no "legally safe" food left. Foods which we have eaten for years could be designated as "unsafe", not because of any change in the composition of the food, but rather because of our advancing abilities to measure the elements of composition in that same food.

Interpretation of new data on carcinogens is also complicated. There is an abundance of new and sometimes-conflicting data on whether or not substances are animal or human carcinogens. Add to that cases of large variations in results between animal species, of positive animal findings coupled with negative human findings, of whether or not tolerance limits exist, etc. Yet there are few, if any, guidelines for sorting out this tangled data for clear and meaningful interpretation.

FDA decisions regarding food safety regulations must still be made in an atmosphere of uncertainty. The decisions would be more equitable, however, if they were based on a scientific evaluation of data and potential hazards using the techniques of risk assessment. This would provide objectivity and consistency in decisions based on "good science" rather than obscure subjectivity. This would also ensure that an adequate review of available data be completed before the regulatory decisions are made.

For these reasons, I support the need to change the definition of "safe" from one based on zero tolerance to one based on insignificant risk. In conjunction, I strongly support the use of risk assessment in analyzing food hazards as a scientific means of determining those substances which present significant risks versus those which present insignificant risks to safety. It's the best tool we have at our disposal.

Chocolate Manufacturers Association
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June 8, 1983

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Honorable Orrin G. Hatch, Chairman
Committee on Labor and Human Resources
SD-428 Dirksen Senate Office Building
Washington, D.C. 20510

Dear Mr. Chairman:

The Chocolate Manufacturers Association and the National Confectioners Association wish to submit a statement for the record on food safety issues currently before your Committee.

Over the past several years bills have been introduced in both the Senate and House of Representatives on food safety. In the 97th Congress, you introduced S.1442 and Representative E. de la Garza (D-Tex.) introduced an identical measure, H.R.4014. Another measure was introduced by Representative Albert Gore, Jr. (D-Tenn.), H.R.5491.

Other documents which have been developed on the food safety issue are the Staff Working Draft Bill of the Senate Labor and Human Resources Committee, and the discussion papers created by the Subcabinet Council Working Group on Food Safety.

We share many of the views on food safety which have been expressed, particularly the need for the food safety program to be credible with the public; that it be relatively efficient; that it not preclude consideration of varied scientific data; and that the federal statutes on food safety be consistent and non-duplicative.

We have several areas of concern, either in the measures introduced in Congress or positions drafted by the Senate Labor and Human Resources Committee staff or the Subcabinet Working Group.

The basic principles involved in our position on food safety for which we recommend the Committee give consideration are as follows:

1. Delaney Clause.

We do not share the view that the Delaney Clause language is as ironclad as often interpreted. We believe there is sufficient room for interpretation based on both the legislative history and the statements of individual FDA administrators. Therefore, we recommend that initially administrative consideration be given to any changes in the Delaney Clause before legislative action is undertaken.

2. Definition of Basic and Traditional Foods.

We find the definition of basic and traditional foods contained in the measures introduced by Senator Hatch (R-Utah) and Representative E. de la Garza (D-Tex.) in the Senate Staff Working Draft to be unacceptable. Should this definition be placed in a statute, it would eliminate many foods from the definition of basic and traditional foods except those lightly processed. Implementation of this definition has the effect of altering a number of current practices — such as the elimination of many foods from priority allocations of gasoline and natural gas in emergency situations; from transportation priorities during emergency periods; elimination of "non basic" foods from certain food classifications under tax laws and in their sale under certain government contracts or programs.

3. Prior Sanction.

Prior sanction was discussed when the Delaney Clause was being considered in 1957, and it became effective January 1, 1958. The prior sanction provision was extended to those substances which had a long and safe historical use in foods. We have not seen evidence — either epidemiologically or from research — which would warrant the elimination of the prior sanction provision. This is not to say that each industry which produces products containing classified substances prior sanctioned would not have the responsibility to determine the safety of these substances, but such actions should not be forced upon the industry unless there is significant research or the epidemiological evidence is sufficient to alter the prior sanction status of that substance.

4. Federal Preemption.

Since most industry products are involved in interstate commerce, it is essential that any regulation involving food safety be established on the Federal level to avoid conflicting state and local regulations.

In conclusion, we are submitting for your comments and consideration a discussion document which outlines our basic position on the best system for bringing about change in the Delaney Clause without sacrificing food safety nor inhibiting the use of the latest scientific research information and methodologies.

We respectively request this statement and accompanying document be made part of the record.

Sincerely,

Richard T. O'Connell
President

RTO:jh

Enclosure

KIRKLAND & ELLIS

MEMORANDUM

TO: Richard T. O'Connell

FROM: James H. Wallace, Jr.
Timothy S. Hardy

RE: Interpretation of the Delaney Clause: Legislative History, FDA Precedents and Current Scientific Knowledge

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As the public dispute over the Delaney Clause in recent years has made clear, much confusion exists about the proper legal standards to apply when a food additive is alleged to cause cancer. FDA precedents on food additives and other substances alleged to be carcinogenic are characterized by conflicting attitudes toward safety evaluation -- often reflecting unstated judgments about the importance of the substance to consumers rather than consistent interpretation of scientific data. The precedents are often also characterized by reliance on the general safety clause of the Federal Food, Drug and Cosmetic Act (FFDC&A) rather than Delaney proscriptions.

Nonetheless, examination of the proper interpretation of the Delaney Clause is central to consideration of how FDA will regulate food additives alleged to be carcinogenic. The Clause's apparently ironclad language -- no additive shall be approved "if it is found to induce cancer when ingested by man or animal" -- must be confronted whenever carcinogenic risks are at issue. At the same time, proper understanding of the Clause, its legislative history, FDA precedent, and current scientific thought about the causes of cancer, emphasize the extent to which the Clause is not in fact ironclad. FDA has in the past been able to modify its interpertation of the Clause when it wished to avoid unwise decisions. Considerable room for such interpretation exists.

In more detail, the legal background against which evidence of tumors in animals fed a food additive can be shown not necessarily to trigger the Delaney Clause relies on:

(1) Changing Definitions of Carcinogens. When the Delaney Clause for food additives was added to the FFD&CA in 1958, Congress, and the scientists who testified before Congress, had in mind a particular definition of cancer, i.e., malignant neoplasms caused by genotoxic substances. Scientific evidence in the intervening twenty years has enriched understanding of cancer so that it can be argued that the concept "cancer" in the Act does not apply to substances found to be associated with animal tumors through mechanisms other than direct genetic damage.

(2) No Cancer Induced. The Delaney Clause applies only to an additive shown to "induce" cancer. In light of

the evidence of the extreme physiologic changes evident in animals in the very high dose animal studies, it can often be argued, given an adequate scientific basis, that any tumors which were produced do not demonstrate that the substance "induces" cancer. Support for this interpretation can be found in FDA's own precedent refusing to apply the Delaney Clause to selenium, where intervening effects of high dosage feeding were found to be the cause of the tumors.

(3) Inappropriate Tests. Many studies used to label substances carcinogenic must meet the second standard set forth in the Delaney Clause, i.e., they must be shown to be "appropriate for the evaluation of the safety of food additives." Two-generation, in utero feeding studies, for example -- at least at very high dosages -- have not been extensively used, have not been validated, and thus are not "appropriate." Similar arguments apply to promotion (and thus not solely ingestion) studies and to implantation studies.

A. Scientific Discretion Under the Delaney Clause.

In considering the Delaney Clause, it must first be emphasized that the Clause does not deprive FDA of scientific discretion. Shortly after its passage, in a letter to the House Commerce Committee, HEW wrote that the Delaney Clause "is not scientifically absolute. [T]he clause allows the exercise of all the judgment that can safely be exercised on the basis of present knowledge . . . It allows the Department . . . full discretion and judgment in deciding whether a substance has been shown to produce cancer."[1/] FDA subsequently has expanded on that interpretation:

> Responsible regulation requires that the evaluation of risk associated with a particular chemical additive must be accompanied by an evaluation of benefit which might derive from use of the material.[2/]

FDA further stated:

> If the only benefit of a food additive is esthetic and the additive is demonstrated to be carcinogenic, no tolerance should be established and the Delaney Clause should be invoked. Where a definite health, economic, and/or nutritional

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[1/] "Color Additives" Hearings Before the Committee on Interstate and Foreign Commerce, House of Representatives, 86th Cong., 2d Sess. (1960) at 500-01 (hereinafter "Color Additives Hearings").

[2/] FDA Delaney Study, reprinted in 1977 Health Hearings at 253, 256. The FDA also stated:

> The expected, intended uses and possible misuses of a material, the length of time in a person's lifetime during which it will be used, the age at which it will be used (e.g., oral contraceptive agents used only during a woman's reproductive years, or drugs used for afflictions of advanced years) and the available alternatives must all be considered in assessing risks. In the evaluation of benefit, the advantage to the ultimate consumer -- probably something concrete beyond pure convenience or improved appearance -- must be the guiding principle.

Id. at 546-47.

> benefit may result from a food additive, it may be in order to attempt to establish a conservative permissable tolerance level in the food supply.[3]

Despite these seemingly flexible interpretations of the Delaney Clause (indicating a willingness even to weigh risks and benefits), FDA has normally not been willing to approve officially those substances believed to be associated with tumors in animals (the notable exception being selenium). FDA's former general counsel, Peter Barton Hutt, has expressed the reasons why there is such an absense of any clear written precedent. He has noted that FDA "in light of the utter ubiquity" of carcinogens and "[f]aced with the increasingly untenable safety requirements of the law, . . . has in many instances simply ignored the evidence of animal carcinogenity of many common food substances and has declined to take action that would be subject to public ridicule."[4]

The general principles of flexible interpretation, however, form an important backdrop to considering the Delaney Clause's applicability, a flexible interpretation with which FDA has recently re-expressed its agreement:[5]

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[3] FDA Delaney Study, reprinted in 1977 Health Hearings, at 651 (emphasis added).

[4] P. B. Hutt, "Public Policy Issues in Regulating Carcinogens in Food," Food, Drug, Cos. L.J. 541, at 549, 550 (1978).

[5] FDA Report to Secretary Califano on the Delaney Clause, 34-35 (1977).

> While this language appears unequivocal, the Act does not define certain critical terms of the Delaney Clause, including those terms which are said to permit the exercise of scientific judgment: "induce," "cancer," and "appropriate for the evaluation of the safety of food additives . . . ." Thus, for example, the statute does not indicate whether, in applying the Delaney clause, FDA is to count benign as well as malignant tumors, or whether it is sufficient that exposure to an additive is associated with an increase in tumors, even though the mechanism of carcinogenesis is the result of some predisposing factor that the chemical has activated. Debate may also arise over the "appropriateness" of particular tests for demonstrating whether an additive does induce cancer in laboratory animals. Clearly, therefore, in the application of the Delaney Clause, scientific judgment was intended to, and does, play an important part.

With these flexible interpretive principles as a background, the remainder of this memorandum reviews the Delaney Clause's legislative history, its use in FDA precedents, and current scientific views on carcinogenicity that argue for even more flexible interpretation in the future.

B. Legislative History of the Delaney Clause

During the first half century of federal food and drug legislation, statutory provisions relating to food safety were quite general. The original 1906 Food and Drug Act merely provided that food shall be deemed to be adulterated:

> If it contains any added poisonous or other deleterious ingredient which may render such article injurious to health.

A similar provision was subsequently included as Section 402(a)(1) of the Federal Food, Drug, and Cosmetic Act, which was enacted in 1938. It has not been amended since.

Following World War II, with the application of scientific technology to the production and processing of food and entry of many new chemicals into the nation's food supply, Congress created in 1950 a Select Committee to investigate use of chemicals in food products. Representative James J. Delaney was appointed Chairman. This Committee held extensive hearings for a year-and-a-half and recommended new legislation to require pre-market safety testing for chemicals.[6/] Although the Committee's report did not deal directly with specific statutory language on "cancer," it did quote testimony from a representative of the National Cancer Institute recommending careful testing for carcinogenic properties in several species of animals prior to approving use of chemicals in food.[7/]

Although the hearings leading up to the 1958 Food Additive amendment began in 1950, no anti-cancer clause was

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6/ H.R. Rep. No. 2356, 82d Cong., 2d Sess. (1952).

7/ The Committee's report was the basis for new legislation to permit FDA to establish tolerances for pesticide chemicals in or on raw agricultural commodities, enacted in 1952 and adding Section 408 to the Act, 21 U.S.C. § 346a. The new pesticide legislation did not contain a cancer clause. Nonetheless, FDA has followed Delaney-type principle with respect to pesticides. See Environmental Defense Fund v. United States Dept. of HEW, 428 F.2d 1083, 1090-92 (D.C. Cir. 1970).

proposed until 1957. In the 85th Congress (1957), however, eight separate bills were introduced dealing with chemical additives in food. Of these, two identically worded bills, H.R. 7798 (Delaney) and H.R. 7938 (Lenore Sullivan, D.-Mo.), specifically provided:

> The Secretary shall not approve for use in food any chemical additive found to induce cancer in man, or after tests, found to induce cancer in animals.

The Secretary of the Department of Health, Education and Welfare (HEW) objected to this provision both because he found it unnecessary:

> No specific reference to carcinogens is necessary . . . since the general requirements of this bill give assurance that no chemical additive can be cleared if there is a reasonable doubt about its safety in that respect.

And because it was too strict:

> Scientists, I am advised, can produce cancer in test animals by injecting sugar in a certain manner, and they can produce cancers by injections into test animals of cottonseed oil, olive oil, or tannic acid (a component of many foods). Probably they can do the same thing with other naturally occurring food chemicals. We think that it would be unnecessary and undesirable to rule out of the food supply sugar, vegetable oils, or common table beverages simply because by an extraordinary application never encountered at the dining table, it is possible to induce cancer by injecting the substances into the muscle of test animals.8/

8/ Quoted in FDA, "Study of the Delaney Clause and Other Anticancer Clauses," ["Delaney Study"] (1974) at 26-27

(Footnote 8 continued on next page.)

As a result, in July 1958, when the House Committee reported a bill on food additives (H.R. 13254), it contained no anti-cancer clause.[9/]

However, subsequent to the filing of the House Report, Congressman Delaney suggested a revised anti-cancer provision, which became the statutory language adopted by Congress:

> Provided, That no additive shall be deemed to be safe if it is found to induce cancer when ingested by man or animal, or if it is found, after tests

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(Footnote 8 continued from previous page.)

(emphasis added). FDA's Delaney Study was submitted in hearings before a subcommittee of the Committee on Appropriations, House of Representatives, 93rd Cong., 2d Session (May 6, 1974) (hereinafter referred to as "1974 Appropriation Hearings").

9/ Congressman Delaney was not without support for his initial proposal which would have banned a substance regardless of the route of administration that had caused the cancer. Dr. W. C. Hueper of NCI told Congress:

> The addition of any chemicals to foodstuffs which possess carcinogenic properties when tested on animals regardless of the route and dose should be prohibited since such additives are bound to increase the carcinogenic load of the consuming public. (Hearings, supra, at 389.)

And Dr. Frances E. Ray of the University of Florida agreed:

> [W]e must in order to maintain a factor of safety, conclude that any substance that causes cancer in any animals by any route of administration must be rejected as a food additive. (Hearings, supra, at 413.)

> which are appropriate for the evaluation of the safety of food additives, to induce cancer in man or animal.

HEW commented on this revised provision and again found it unnecessary. But, HEW said, the Clause was acceptable as reworded:[10]

> Any indication that the additive may thus be carcinogenic would, under the terms of the bill [and without the Delaney Clause], restrain the Secretary from approving the proposed use of the additive unless and until further testing shows to the point of reasonable certainty that the additive would not produce cancer and thus would be safe under the proposed conditions of use.

Although it viewed the provision as unnecessary, HEW thus did not specifically object to inclusion of the Delaney Clause.

The Department also made it clear that the revision was important as it eliminated the strict wording of the originally proposed clause which HEW again noted, "would, if read literally, forbid the approval of use in food of any substance that causes any type of cancer in any test animal by any route of administration."[11]

The Food Additives Amendment passed both the House and Senate with the revised Delaney Clause. The Senate Report stated however:[12]

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[10] FDA Delaney Study at 30.

[11] Id.

[12] S. Rep. No. 2422, 85th Cong. 2d Sess. (1958) (emphasis added).

C. Prior FDA Reliance on the Delaney Clause

For a number of reasons, FDA has rarely invoked the Delaney Clause. First, in the food context, the Delaney Clause is applicable only to food additives, substances intended to become, directly or indirectly, part of food. The definition specifically excludes GRAS substances and prior-sanctioned ingredients.[14/] Similarly, the color additives Delaney Clause applies to permanently listed, rather than provisionally listed, colors.[15/] Further, the Agency has typically elected to proceed under the general safety provisions when a finding of carcinogenicity is a possibility rather than a probability.[16/] The few times FDA has relied on Delaney are described below.

(Footnote 13 continued from previous page.)

> We must consider the chemicals that are under study in terms of their use in food products and their potential use by consumers, not in abnormal doses . . . in animals. (Hearings, supra, at 375.)

[14/] See FDA's decisions regarding safrole, 25 Fed. Reg. 12412 (December 3, 1960); calamus, 33 Fed. Reg. 6967 (May 9, 1968); and cyclamates, 34 Fed. Reg. 17063 (October 21, 1969).

[15/] Thus, in the cases of Violet No. 1, 12 Fed. Reg. 9077 (April 10, 1973), Red No. 2, 41 Fed. Reg. 5823 (February 10, 1976, and Yellow No. 1, 42 Fed. Reg. 62482 (December 13, 1977), FDA did not act under the color additives Delaney Clause.

[16/] See FDA decisions regarding diethylpyrocarbonate (DEPC), 37 Fed. Reg. 3060 (February 11, 1972), and 37 Fed. Reg. 15426 (August 2, 1972); mercaptins, 38 Fed. Reg. 10116 (April 24, 1973), and 38 Fed. Reg. 33072 (November 30, 1973); acrylonitrile, 42 Fed. Reg. 13546 (March 11, 1977).

FDA's first formal invocation of the Delaney Clause came in the case of Flectol H, a component of food packaging adhesives.[17] FDA revoked the food additive regulations governing Flectol H, stating only that:

> The Commissioner of Food and Drugs has evaluated newly received information reporting that the substance induces cancer when ingested by test animals and concludes that the food additive regulations should be amended to delete provision for use of said substance.

In late 1969, FDA revoked the food additive regulation governing chloroaniline, a component of food contact articles. FDA's narrative reasons for the revocation paralleled its Flectol H decision.[18]

In 1976 FDA proposed to remove chloroform from use in food on the ground that a National Cancer Institute study demonstrated that it induces liver cancer in mice and renal tumors in male rats.[19] In so doing, it specifically invoked the Delaney Clause.

In September 1977, FDA proposed to revoke the food additive regulations governing trichloroethylene (TCE), on the ground that a National Cancer Institute report found hepatocellular carcinomas in mice at high dose levels, although none were found in rats.[20] However, because FDA found (1) no data showing TCE to be a human carcinogen, (2) that TCE is greatly diluted in food, and (3) only small amounts remain in packaging, and "only a vanishingly small amount of TCE could migrate into food" from this packaging, FDA did not issue public warnings on TCE, and permitted its last stocks to be used. FDA has never issued any final revocation.

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[17] 32 Fed. Reg. 5675 (April 7, 1967).

[18] 34 Fed. Reg. 19073 (December 2, 1969).

[19] 41 Fed. Reg. 15029 (April 9, 1976).

[20] 42 Fed. Reg. 49465 (September 27, 1977).

Similarly, FDA proposed to prohibit the use of 2-nitropropane in food on the ground of its carcinogencity, but has not issued a final regulation.[21/] FDA did not specifically cite the Delaney Clause in this proposal, probably because the results were achieved after inhalation testing. As in the case of TCE, FDA's 2-nitropropane proposal does not require immediate removal of the substance from the food supply, and permits use of existing stocks, because no data had been adduced showing human carcinogenicity and "only small amounts of 2-nitropropane remain in food packaging adhesives from its regulated use."

FDA also proposed to prohibit the use of hydrazine in food, but once again no final regulation has been issued.[22/] In this instance, FDA specifically stated that it acted under the Delaney Clause, after the International Agency for Research on Cancer reported that "oral administration of

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[21/] 43 Fed. Reg. 56247 (December 1, 1978).

[22/] 44 Fed. Reg. 33693 (June 12, 1979).

Commissioner Goyan's cyclamate decision, however, perhaps well reflects the way FDA viewed food additive carcinogen issues in the last Administration. The decision explicitly relies, not on the Delaney Clause, but rather the general safety clause, despite denying food additive approval because cyclamate had not been shown not to be carcinogenic.[27/]

FDA precedents themselves (with the exception of the selenium decision to be discussed below) thus offer little assistance in developing a flexible interpretation of the Delaney Clause. Consideration of the Clause's legislative history in the perspective of modern understanding of cancer and its causes, as described next, however, provides strong arguments for holding FDA to its flexible interpretations as described in Section A of this memorandum above.

D. Growing Sophistication About the Etiology of Cancer

The Delaney Clause is premised on a particular understanding of what it means for a substance to "induce cancer." The evidence presented to Congress that led it to enact the Delaney Clause, and the justifications made for the Delaney Clause ever since, are premised on the assumption that there is no substantial scientific evidence to establish tolerances for ingestion exposure to carcinogenic substances. With this scientific background in mind, Congress declared

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[27/] 45 Fed. Reg. 61474 (Sept. 18, 1980).

it to be national policy not to allow any substance that causes cancer at any dose level in any valid ingestion study (in man or animal) to be a food additive. Thus, what Congress thought it was talking about when it put a special provision for "cancer" in the 1958 Amendments is relevant to interpretation of the Delaney Clause today.

The testimony presented during the hearings leading to the 1958 Food Additives Amendments indicates that in enacting the Delaney Clause Congress adopted the scientific arguments presented that cancer was at that time (a) not well understood, (b) irreversible, and (c) caused by substances for which no safe dose can be determined.

Dr. W. C. Hueper, Chief of the Environmental Section of the National Cancer Institute, for example, made clear the lack of understanding of the cancer mechanism in indicating that scientists really had no good definition of a carcinogen.[28/]

> A carcinogen is a substance which, under certain conditions when applied to a man or experimental animals will produce cancer which otherwise would not have occurred. It is a rather broad definition. It is perhaps the best definition we have at the present time.

Both Dr. William E. Smith, a medical researcher from Harvard, Rockefeller and Sloan-Kettering, and Dr. Heuper, discussed the "peculiar pharmacology of carcinogens," noting

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[28/] Hearings before a Subcommittee of the House Committee on Interstate and Foreign Commerce on Bills to Amend the Federal Food, Drug and Cosmetic Act with Respect to Chemical Additives in Food, 85th Cong. (1958), at 371.

that unlike many toxic substances the effects of carcinogens are irreversible. Dr. Smith said, "carcinogens have the unusual property of inducing irreversible changes in living cells, so that the cells slowly progress to cancer long after treatment with the chemical is stopped." He added it does not always take many exposures to induce cancer:

> Many scientists have induced cancer late in the life of animals by giving them, when young, a single dose that could be put on the head of a pin.

Dr. Hueper made it clear he felt science could not determine a threshold level of safety for a carcinogen:[29/]

> I do not think we have the method or evidence available by which we can reliably determine a safe dose . . . . So we are still in the twilight area in which we do not know exactly when and where a safe dose for an environmental carcinogen may be placed.

These views were consistent with those of the general scientific community at the time. For example, the Joint FAO/WHO Expert Committee on Food Additives stated in 1961:[30/]

> It is known that various factors may be involved in carcinogenesis, including chemical agents, ionizing radiations, hormonal imbalances and viruses, but the mechanism is not completely understood. . . . In the

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29/ Id. at 372. See also Hueper testimony at 388-80 and testimony of Dr. Herbert E. Carter of the Department of Chemistry and Chemical Engineering at the University of Illinois (Hearings, supra, at 376); and letter of Dr. Smith, 1957 Cong. Rec. A1352.

30/ "Evaluation of the Carcinogenic Hazards of Food Additives" at 18 (1961).

> instance of certain food additives or contaminants reported to be carcinogenic (e.g., aminotriazole) it is thought that a hormonal mechanism is involved. In this case it has been suggested that such an agent should be called an "indirect carcinogen. No useful practical purpose appears to be gained by such a distinction at the present time.
>
> It has been demonstrated, under certain experimental situations, that carcinogenesis may be a two-stage process involving an "initiator" and a "promoter" which may be separate agents. This aspect of carcinogenesis is so far insufficiently understood or generalized to be considered in the present practical context.

If a clear line can be drawn between those common characteristics of "cancer" and of carcinogens as described to Congress in the 1950's and current understanding of these concepts, it can be argued that a food additive that is associated with tumors in animal feeding studies should not automatically be treated as a "cancer inducer" under the Delaney Clause.[31]

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[31] FDA's Dr. Albert C. Kolbye has described the scientific questions relevant to such an argument:

> Here is a brief review of some of the major points of scientific controversy:
>
> What is the scientific definition of a carcinogen?
>
> Is this coincidental with the same considerations involved with "inducing cancer?"

(Footnote 31 continued on next page.)

The conceptual sophistication about cancer that has emerged since 1958 is substantial. As Dr. R. Kroes of the Central Institute for Nutrition and Food Research, Zeist, the Netherlands, has written:

> If a carcinogen is defined as a compound which is able to induce development of cancer, it must be emphasized that this definition is only based on biological result, and not on the actual mechanism of action. This means that complete carcinogens (i.e. compounds acting on the genes of the organisms, the so-called genotoxic compounds) as well as compounds acting through a different (indirect)

(Footnote 31 continued from previous page.)

> Do we mean "cause," "a potential cause," "elicit," "lead into," "bring about," "effect," or "affect" cancer incidence?
>
> Said a different way: does any exposure to any substance that can modify the expression of tumors in test animals upwards make that substance a "carcinogen," or more specifically constitute sufficient evidence of ". . . found to induce cancer . . . ."
>
> Should we differentiate factors that appear to influence the expression of cancer when fed to animals at high dose levels but which do not appear to be "initiators" of cancer in terms of current experience from other agents more likely to act as tumor promoters?

"Decision-Making Issues Relevant to Cancer Including Substances," at 6-7, presented at the Conference on the Scientific Basis for Interpretation of the Delaney Clause (Washington, Feb. 6-8, 1978) (paragraphing supplied).

> mechanism (e.g., hormones, immunosuppressants, co-carcinogens, promoters) come within this definition.[32]

Kroes goes on to point out that definition of carcinogenicity in terms of mechanism, rather than "biological result" yields a substance continuum upon which one can find safe-threshold substances. If, as seems reasonable in light of the legislative history, the intent of Congress in the Delaney Clause was to define cancer in terms of mechanism rather than biological result, then it can be argued the Delaney Clause applies to only that portion of the "Kroes continuum" that he refers to as complete carcinogens.

Dr. Albert Kolbye, FDA Associate Bureau Director for Toxicology and Assistant Surgeon General, agrees with the importance of distinguishing carcinogens on the basis of their mechanism of action. He recently questioned "whether compounds that create risk for cancer by a promoting or modifying action without significant initiating action should be called 'carcinogens.'"[33] He noted that regulation will become increasingly difficult if promoters and modifiers are labeled carcinogens, because many natural ingredients in foods would then be classified as carcinogens.[34]

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[32] R. Kroes, Evaluation of Results of Animal Data with Respect to Extrapolation, Health and Sugar Substitutes 272 (Geneva 1978).

[33] Memorandum, Kolbye to FDA Commissioner, July 25, 1980, at 2.

Kolbye suggests therefore that alleged carcinogens should be classified into two categories:

> (1) "First Order" substances, which induce cancer at subtoxic doses, because they are either effective initiators or complete carcinogens; and
>
> (2) "Second Order" substances, which influence cancer induction either by activating endogenous electrophiles, causing hyperplastic toxicity, or decreasing biological resistance to independent forms of cancer induction.

Kolbye concludes that Second Order compounds should not be deemed carcinogens "even though under some circumstances and at some doses they may be powerful driving forces that can substantially influence cancer induction."[35]

In sum, today's greater sophistication about cancer and its causes establishes a scientific basis for interpretation of animal feeding studies that should lead FDA not to invoke the Delaney Clause whenever tumors are found in treated animals. As scientists, including Dr. Kolbye of FDA, have argued, distinctions need to be made between direct initiators of cancer and substances that through other mechanisms affect tumor development.

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[34] *Id*. Kolbye observed "the action of most promoters and thereby an increased risk of cancer are attained only after repetitive dosing at very substantial levels" whereas initiators induce malignancy at doses significantly below toxicity. *Id*. at 3.

[35] Kolbye, *The Application of Fundamentals in Risk Assessment*, presented in June 1980 to the Pesticides Division of the American Chemical Society.

E. The Requirement That a Substance be Shown to "Induce" Cancer

The argument that the Delaney Clause does not apply to many alleged carcinogens has grown not only out of a more sophisticated understanding of cancer, but also from the fact that the Delaney Clause requires proof that a food additive "induces" cancer. Although neither the legislative history of the Delaney Clause,[36] nor subsequent interpretation of the Clause by FDA or the courts has shed much illumination on the meaning of "induce," strong arguments exist that the word is intended to encompass only the direct causation characteristic of the classic genotoxic carcinogens of which Congress was thinking in 1958.

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[36] Some indication, however, of the limits on what will be found to have "induced" cancer can be found in analogous legislative history. In testifying at the hearings leading to the inclusion of a Delaney-type clause in the Color Additives Amendment, the Secretary of HEW noted:

> It has been suggested that once a chemical has been shown to induce a tumor in a single rat, this forecloses further research and forever forbids the use of the chemical in food. This is not true. The conclusion that an additive "is found to induce cancer when ingested by man or animal" is a scientific one. The conclusion is reached by a competent scientist using widely accepted scientific testing methods and critical judgment. An isolated and inexplicable tumor would not be a basis for concluding that what the test substance produced is cancer.

Color Additives Hearings, at 62 (1960) (emphasis added).

Many alleged carcinogens are not genotoxic. That is, they do not bind to DNA, nor metabolize to any other compound that might bind to DNA, and are not mutagenic. Thus, the scientific evidence supports strongly arguments that, whatever may be the meaning of the tumors such chemicals may be associated with at high doses, it is not that they "induced" cancer.

The FDA has concurred in this rationale for carcinogen assessment in its selenium decision. In finding that the Delaney Clause should not be applied to determination of whether selenium could be added to animal feed, FDA stated:[37]

> In three of the six studies available on the subject, test animals were found to have developed neo-plastic lesions.
>
> [However] These lesions were concluded to be a consequence of liver cirrhosis produced by frank selenium toxicity.

The FDA further discussed the selenium decision in its 1974 Delaney Clause Report:[38]

> If a food additive causes a pathologic change at a particular level (e.g., liver damage), and it is that pathologic change (rather than the additive directly) which in turn leads to cancer, the anticancer clause does not preclude approval of that additive for use at levels which provide an adequate margin of safety below the point at which it causes the pathologic change involved.

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[37] 38 Fed. Reg. 10458 (April 27, 1973).

[38] FDA Delaney Study at 47.

FDA's Dr. Albert Kolbye has more recently questioned the efficacy of high dose testing, because high doses "may invoke a broad variety of indirect factors that either potentiate the carcinogenic potency of electrophilic initiators, . . .or decrease the biological resistance of test animals . . . ."[39] He continued:

> Another way to approach the problem is to ask whether we should assume that high exposure levels to chemicals, sufficient to cause gross toxicity or metabolic distortion in the test animals, will more likely increase the risk for cancer induction than not.

Despite the selenium precedent, FDA has on other occasions evidenced an unwillingness to accept such arguments about intervening factors "unless there is a clear and thorough understanding of specific metabolic or other physiological factors which define such test conditions as inappropriate."[40] Nonetheless when a sufficient scientific basis has been established to show that a substance does not directly induce cancer, arguments such as those employed by FDA in the selenium decision should preclude reliance on the Delaney Clause.

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[39] Kolbye, Impact of Short-Term Screening Tests on Regulatory Action, presented at the Workshop of The Scientific Council of the Netherlands' Cancer Society, at 6. (April 1980)

[40] FDA Delaney Study at 745.

The NAS Saccharin Report (Part I, at 3-14) indicates that there is an open question whether the Delaney Clause applies in some such situations by asking:

> Does the Delaney Clause, which prohibits FDA from approving additives that "induce" cancer, thereby prohibit FDA from approving cancer promoters?

F. The Appropriateness of Unvalidated Cancer Studies.

The second phrase of the Delaney Clause states that a food additive may not be used "if it is found, after tests which are appropriate for the evaluation of the safety of food additives, to induce cancer in man or animal." The legislative history of the Delaney Clause includes limited Congressional consideration of which tests are appropriate for concluding that a substance will cause cancer in man. HEW, for example, raised the issue of injection testing, stating that such testing would not be appropriate for determining the carcinogenicity of a substance:

> Concentrated sugar solution, lard, certain edible vegetable oils, and even cold water have been reported to cause a type of cancer at the site of injection when injected repeatedly by hypodermic needle into the same spot in the test animal. But scientists have not suggested that these same substances cause cancer when swallowed by mouth.41/

41/ Quoted in FDA's Delaney Study at 30.

FDA Commissioner Alexander Schmidt agreed, noting that even salt causes cancer in rats, at high doses, because "[p]ractically any chronic irritant can cause cancer." 1974 Appropriations Hearings at 288.

Other scientists referred to alternative administration routes, including application to the skin.[42]

However, Congress did not expressly consider the appropriateness of two-generation, in utero animal feeding tests, because such tests were not widely used at that time.[43]

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[42] For example Dr. Herbert E. Carter of the University of Illinois noted cancer studies where there was "application to the skin or injection into the bladder or under the skin," and commented:

> [N]o one would in any wise recommend that a substance established to be a potential carcinogen under these circumstances [n]ever be considered as a food additive.

Dr. William B. Deichmann, Chairman of the Department of Pharmacology at the University of Miami School of Medicine agreed:

> I see no reason to reject a compound considered as a food additive for the sole reason that it produced skin cancer in a hypersensitive mouse.

Hearings before a Subcommittee of the House Committee Interstate & Foreign Commerce, 85th Cong. (1958), at 376, 384.

[43] A few scattered references to in utero exposure were made during the Congressional hearings. For instance, Dr. Hueper noted as part of a general description of the dangers of lifetime low dose exposure to carcinogens:

> Experimental observations indicate the possibility that contact with carcinogenic chemicals may affect the fetus during intrauterine life through penetration of these chemicals from the mother through the placental barriers to the fetus.

Id. at 387.

(Footnote 43 continued on next page.)

The FDA has subsequently made the following interpretation of the differences between the two clauses of the Delaney Amendment:

> The clauses differentiate between an additive found to induce cancer when ingested by man or animal, and one found to induce cancer after tests involving application or administration other than by ingestion. The clauses require that the additive be banned if cancer is induced by ingestion. . . .
>
> Thus, any test other than oral feeding requires scientific judgment as to whether it is an appropriate test to determine carcinogenesis. This means that such test methods as gavage (intubation), injection, implantation, and others would not automatically result in application of the anticancer clause even upon a finding that they induce cancer.44/

Despite the paucity of Congressional consideration or guidance about such tests, the appropriateness of such tests must be measured against current generally accepted principles of testing. Recent statements by scientists and by FDA, in hearings and in decisions, as well as decisions by

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(Footnote 43 continued from previous page.)

Also, Dr. Ray submitted into the record the recommendations of the 1956 Rome Symposium of Potential Cancer Hazards which stated:

> Food additives should be permitted only if . . . through at least 2 generations in at least 1 suitable species they have no toxic effect.

Id. at 413.

44/ FDA Delaney Study at 209.

other agencies concerned with cancer testing, are instructive on the issue of "appropriate" non-ingestion tests.

FDA has identified, on a case-by-case basis, certain experimental practices which, in its view, render non-ingestion tests unreliable. An example is the series of experiments conducted on the color additive FD&C Red No. 4.[45] In those experiments, dogs that consumed the color additive developed lesions in the urinary bladder. Because it was unclear whether the color additive or the repeated catheterization performed on the dogs in the course of the tests had caused the lesions acting FDA Commissioner Gardner found the tests inconclusive and ordered additional studies.

In the Citrus Red No. 2 order, the FDA held that implantation or injection was not an appropriate method for carcinogenic testing. Instead, long range feeding studies should monitor the results of consumption by ingestion.

In a recent "Talk Paper" issued by the FDA, a study of formaldehyde inhalation by rats, which concluded that such inhalation causes tumors in the nasal passage, was not deemed probative of the effect of the chemical on humans.[46] Similar studies using mice displayed no incidence of tumors, and the FDA ordered additional tests to determine if human reaction to formaldehyde approximates that of mice or rats.

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[45] 41 Fed. Reg. 41852 (Sept. 23, 1976).

[46] Food Drug Cos. L. Rep. (CCH) ¶ 909 (1980).

In sum, any studies other than traditional one-generation ingestion studies must be carefully assessed as to their appropriateness to determining food additive safety before being relied upon to invoke the Delaney Clause. It is clear the Congress and FDA have always considered injection, implantation and skin painting studies to require such validation before being considered appropriate for such evaluation. In addition, however, the increasingly used two-generation, in utero exposure bioassays, promotion studies where more than one substance is fed animals, and the wide variety of short term studies, must all be assessed for their appropriateness for safety evaluation. Considerable sentiment exists in the scientific community for putting limited reliance on such studies, and thus "positive" results in any such study should not necessarily invoke the Delaney Clause.

Howard R. Roberts
9302 TALISMAN DRIVE • VIENNA, VIRGINIA 22180

June 7, 1983

Ms. Barbara Souder, Staff Assistant
Committee on Labor & Human Resources
SDOB 428
United States Senate
Washington, D.C. 20510

Dear Ms. Souder:

Dr. John Doull asked that I submit, for the record, on his behalf the following articles:

J. Doull, "Food Safety and Toxicology,"
in H.R. Roberts (Editor), Food Safety,
John Wiley & Sons, Inc., New York (1981)

H.R. Roberts, "Food Safety in Perspective,"
in H.R. Roberts (Editor), Food Safety,
John Wiley & Sons, Inc, New York (1981).

These articles are submitted in lieu of Dr. Doull's personal appearance on June 9, 1983, before the Senate's Labor and Human Resources Committee Food Safety Hearings.

Sincerely,

Howard R. Roberts

HRR:mc

Enclosures

cc: Dr. John Doull

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CHAPTER 1

Food Safety in Perspective

H. R. ROBERTS

Newspaper and magazine articles, television and radio reports, scientific and technical literature, government activity, and public opinion polls all bear witness to a current preoccupation with the nature and the safety of our food supply. We are constantly being told that certain components of our food and what and how much we are eating are jeopardizing our health. For example, in recent years a wide variety of popular books, as well as government reports, have focused on such issues as the controversy over food additives, the role of diet in children's hyperactivity and in heart disease and cancer, and the importance of vitamins (e.g., 1–11). Best-seller lists are seldom without one or more entries representing the latest diet [e.g., the Scarsdale (12) and Pritkin (13) diets]. Even Dr. David Reuben, who explained everything we wanted to know about sex, quickly turned his attention to nutrition (14). Congress, not often in the habit of avoiding areas of popular attention, has repeatedly entered the fray. In addition to addressing the saccharin and nitrite issues, congressional activity has ranged from the recommendation of national dietary goals (15)—inspiring debate in the nutrition community (16)—to a general examination of food safety policy (17). Then, too, scientists, once content to subject preliminary findings to peer review and further research, in some cases now seek popular notice of their unsubstantiated conclusions—finding ready allies to that end in the media and adding to the concern about our food supply (18).

Our preoccupation with food safety has grown along with and has been reenforced by fairly significant changes in the nature of our food supply, especially those that have occurred over the last 20 years or so. In that period the shift of the population to urban areas has continued, accompanied by a concentration and a mechanization of agricultural production. Today, less than 5% of our population produces not only the food consumed by our generally well-fed citizens, but also significant surpluses used in other parts of the world. This highly efficient production system, together with equally efficient processing and distribution systems, has not only provided the convenience and variety of foods demanded by current lifestyles, but has also generated a wide variety of protest.

Of the nearly $200 billion worth of food consumed annually, about 55% is subjected to some processing before distribution. This level of food processing is largely responsible for the variety of food items—on the order of 5000 to 10,000 in today's supermarkets—and for the convenience and the uniformity of quality associated with current lifestyles. Another facet of today's lifestyles is reflected in the expenditure of over one-third of our food dollars on prepared foods purchased and/or consumed away from the home. Trends seem to indicate further increases both in the proportion of processed foods and in away-from-home purchase and consumption. Another trend is the increasing personal interest in nutrition. There are probably few families in the United States in which at some time at least one member is not dieting to gain weight, to lose weight, or to avoid "additives" or other dietary components (e.g., vegetarianism).

On the one hand, the trends in the nature of our food supply have been encouraged by consumer acceptance of the results. At the same time, however, there is some dissatisfaction with highly processed foods and a yearning for the "good old days" when foods were prepared "from scratch." [R. L. Hall, in an article entitled "Faith, Fad, Fear and Food" (19), discusses the assertion that the craze for health foods is a substitute for conventional religion.]

FOOD SAFETY IN HISTORY

Although current concern about food safety is a relatively recent phenomenon, safety problems in the food supply go back to the origins of *Homo sapiens*. Indeed, the first toxicologist was probably the prehistoric person who deduced that unknown plants and fruits were safe to eat if they were consumed without obvious harm by animals. (It is interesting to note that millions of years later we are still making food safety decisions on the basis of effects observed in animals, except that now we are infinitely more sophisticated about looking for those effects.) Observation of the animals left something to be desired, however. As Tannahill (20) has noted, neanderthal people, dependent on hunting, fishing, and plant collecting for their food, were subject to vitamin deficiencies, seasonal malnutrition, plant poisons, and contaminated food.

Lacking any means of preservation, prehistoric people apparently consumed meat left over from the hunt with little, if any, concern for decomposition or its effects on mortality. Later, the value of freezing and drying—climate permitting—and smoking was recognized for preserving meat and fish. Still later the use of salt became a common preservation technique for these products but for other products proper preservation remained a problem for thousands of years.

In addition to the early preservation techniques, another precursor of modern food processing, cooking, was probably in existence in neolithic times. The earliest food additives, salt and smoke, were in use in this era, and others were added when fermentation was discovered and the first simple breads, beers, and wines came into being. Despite improvement in variety, taste, and palatability, though, nutrition and food contamination problems remained.

Convenience foods also go back to prehistoric times, at least in terms of dried foods. Dried snake was a favorite of Chinese travelers more than 2000 years ago. The Tibetan favorite was likely their powdered tea and yak butter mixture (20). Thousands of years later, in the time of Columbus, dried beef and pork and hardtack were the staples for sea voyagers, for whom, among various nutrition problems of that day, scurvy was especially a problem. The introduction of lemons (providing vitamin C) amelioriated the problem and incidentally was one of the first instances of the nutrient fortification of the diet.

Much of the history of humans from the point of view of food safety involved the problems of spoiled and contaminated foods. Thus it is not unexpected that spices would play a major role in the food supply. Spices were among the first food additives used and were important not only to enhance the taste of foods, but also to disguise the taste of spoiled foods. The spice trade was an important factor in world history at least from 1450 B.C. in Egypt throughout the era of the Roman Empire and into the middle ages (20).

With the advent of the industrial revolution, food safety problems were multiplied by increasing urbanization and the age-old problems of nutrition and food spoilage and contamination. The deliberate adulteration of food also increased significantly in this period. Adulteration ranged from the relatively harmless practice of mixing floor sweepings with pepper, ash leaves with tea, and mahogany sawdust with coffee to the addition of copper to pickles, picrotoxin to beer, prussic acid to wine, and lead and copper salts to sweets. Such adulteration became a public issue and probably provided some historical basis for the currently unfavorable, but popular perception of food additives (21).

One of the most significant events in the history of food safety was the initial development of the canning process by Nicolas Appert in 1809. Appert, vying for a prize of 12,000 francs offered by the French government, succeeded in preserving various foods in stoppered glass bottles heated in boiling water. The microbiological explanation of why this approach worked was not to be known until many years later, but Appert's basic approach is that used today in commercial canning (22). The food safety problems involved in improper heat processing of foods will form an important part of our subsequent discussion.

FEDERAL FOOD LAW

As the twentieth century dawned, several states had "pure food" laws, but it took the unstinting efforts of Dr. Harvey Wiley and his "poison squad" to secure passage of the first federal law in 1906 (23, 24). The pure food and drug law of 1906 reflected the simple belief of that time that food was either pure or adulterated. Although amended several times, the changes most pertinent to our food safety discussion occurred in 1958. The 1958 amendments not only shifted the burden of demonstrating the safety of food additives to industry, but also contained certain features that have contributed to today's concern about food safety. Most important is the so-called Delaney Clause, which forbids the use of any food additive shown to induce cancer in humans or animals. Another feature was the "grandfathering" of additives in use at the time through the exemption for generally recognized as safe (GRAS) substances. Subsequently, the banning of cyclamates brought a presidential directive to review the safety of the GRAS substances. The GRAS review initiated in 1970, in part and in turn, has led to the Federal Food and Drug Administration's (FDA's) cyclic review of all direct and indirect additives, now in process. Revisions to the Federal Food, Drug, and Cosmetic (FFD&C) Act have also tightened regulatory control of the safety of color additives (in 1960) and drugs used in food-producing animals (in 1962 and 1968). Interestingly, the trend toward stricter legislative control of food safety was interrupted in 1976 by the vitamin amendments to the act. These amendments were directed at limiting FDA control over composition, labeling, and use of vitamin supplements (25). The current FFD&C Act (26) is in many ways a loosely integrated collection of independent approaches to the various aspects of food safety and is frequently cited in the following chapters of this book.

In the generation since the 1958 Food Additives Amendments, science has made a quantum leap forward, with analytical chemistry increasing the sensitivity of detection from tenths of a percent to parts per billion and, in some cases, parts per trillion. This increase in the sensitivity of detection has produced evidence of trace contaminants in food that were hitherto unsuspected and has raised the fundamental question of the significance of such minute amounts to food safety. Toxicology, too, has advanced with evermore exquisite searching for adverse effects in animal studies and the addition of the new branches of genetics toxicology and teratology. With these advances, science has augmented the inherent concern about food safety and consistently reproves the theorem that absolute safety of the food supply is impossible.

THE RISKS FROM FOOD HAZARDS

All of this brings us to the basic question of this book: "Is our food supply safe?" Strictly speaking, the answer must be "no," since safety implies the absence of hazard or risk (27, 28). Much like all other aspects of life, absolute food safety is impossible for there is virtually no component of our food supply that is without some risk to some part of the population. What are those risks, then? That question has a complicated set of answers that can best be provided by an overall examination of the several areas of hazards associated with our food supply and the relative risks that they present to human health. [For an excellent discussion of the scientific assessment of these risks, the 1978 report of the Food Safety Council (28) is recommended.]

The various types of hazard associated with the food supply can be grouped in several different ways. For any such grouping, the evaluation of risk involves three major criteria: severity, incidence, and onset. *Severity* indicates the type of effect involved, ranging from mild and temporary discomfort through more serious but reversible effects, to irreversible effects, including death. *Incidence* refers to the number of cases or rate of occurrence of a given effect. *Onset* denotes the time of occurrence of the effect after exposure to a hazard and can range from immediate to long term (29).

Quantification of the three risk criteria presents different degrees of difficulty. In certain cases direct human observation is possible, but in most cases there is only anecdotal or indirect evidence based on human experience, epidemiology studies, or laboratory studies with animals or other test systems. Nonetheless, a relative ranking of risks can be made for the various areas of food safety, and a practical perspective can be gained on the total food safety problem by examining each resulting area.

Applying the risk criteria of severity, incidence and onset and grouping food safety hazards into five convenient classes result in the following ranking from greatest to least risk: (*a*) foodborne hazards of microbial origin, (*b*) nutritional hazards, (*c*) environmental contaminant hazards, (*d*) food hazards of natural origin, and (*e*) food and color additive hazards.

Although the public conception of food risks is generally in reverse order, or as Hall (30) has said, perverse order, to this ranking it has been presented and discussed a number of times by Wodicka (31), Hall (32), and Schmidt (33) and is consistent with the thinking of most food technologists. For example, the conclusions of the Marabou Symposium on Food and Cancer (34) was the following:

> Of the potential sources of harm in foods the largest by far are, first, microbiological contamination and, next, nutritional imbalance. Risks from environmental contamination are about 1,000 times less and risks from pesticide residues and food additives can be estimated as about a further 100 times smaller again. Naturally occurring compounds in food are far more likely to cause toxicity than intentional food additives.

The particular classification and ranking just noted formed the basis for an American Institute of Nutrition symposium on food safety in 1978 (29, 35–38), from which the idea for this book originated.

The rationale for this approach to characterizing food safety is presented for these five areas in order of their risk in Chapters 2 through 6, respectively. Briefly, though, to set the stage, the five chosen risk categories encompass the following considerations.

Foodborne Hazards of Microbial Origin

It is well known that foods can serve as vehicles of many pathogenic and toxigenic agents of disease. Foodborne disease agents are characterized by their diversity. Some produce their effects through toxic metabolites resulting from growth of the organisms in the food prior to ingestion (e.g., staphylococcal food poisoning and botulism). Others produce adverse effects through ingestion of living organisms (e.g., *Salmonella*). Still others require the ingestion of large numbers of living organisms that sporulate in the digestive tract and release a toxin (e.g., *Clostridium perfringens* poisoning). The source of these hazards may be on the farm; during food processing; or, more likely, during food service preparation or preparation in the home. The importance of this area prompted a special report in 1975 on microbial hazards in foods by the National Academy of Sciences (39).

The severity of microbial effects ranges from temporary discomfort and rather prompt recovery to the acutely toxic effects of botulism, which, depending on the speed of diagnosis and treatment, can have a very high mortality rate. [Botulinum toxin is the most powerful poison known to humans, with the oral lethal dose estimated to be between 0.1 and 1.0 μg (40)]. Even the normally less dangerous foodborne diseases can have very severe effects, perhaps contributing to death in the case of infants, the elderly, and debilitated persons. Incidence of foodborne diseases as reported to the Federal Center for Disease Control in Atlanta amounts to only a few thousand cases annually, yet the total number of cases may be on the order of 10,000,000 annually (41). The time of onset for the foodborne diseases is fairly immediate. For example, in the case of botulism, symptoms begin to appear within 12 to 36 hours after ingestion of food containing the toxin. Staphylococcal food poisoning generally appears within 1 to 6 hours after the food is ingested, and salmonellosis occurs within 12 to 18 hours after the organisms are ingested.

Nutritional Hazards

The hazards in the food supply associated with nutritional factors can be thought of in terms of both deficiencies and excesses in nutrient intakes. Such nutritional deficiency diseases as scurvy, pellagra, rickets, beriberi, and goiter illustrate the hazards associated with nutrient deficiencies. Some of these were prevalent in the United States early in the twentieth century until they were largely irradicated through improved dietary intake and the nutrient fortification of staple foods. Some still exist in underdeveloped parts of the world. At the other end of the spectrum the toxicity of excess doses of the fat-soluble vitamins in particular is well known (42), as is that of some of the trace elements (43). In addition to the deficit and excess ends of the spectrum, there are various concerns associated with poor nutrition. For example, increased susceptibility to infectious diseases, to foodborne diseases, and to the effects of environmental contaminants arising from malnutrition immediately come to mind. Further, information is gradually evolving in regard to the adverse effects of poor nutritional status at various stages of human development on the etiology of chronic diseases. Of special concern is the increasing prevalence of self-prescribed megavitamin therapy—especially in light of existing knowledge of the toxicity of the fat-soluble vitamins and growing concern about the water-soluble vitamins. Similarly, the Food and Nutrition Board (44) specifically has warned against habitually exceeding the upper intake levels listed for the trace elements because of potential toxicity. Finally, and perhaps most importantly, the continuing appeal of fad diets presents significant potential for hazard, as illustrated by the problems arising from the sole use of certain liquid-protein diet preparations (45).

Thus, although the hazards associated with nutrition are of varying severity, collectively they must be considered of major significance. The incidence of nutritional hazards is difficult to quantitate. Nutritional deficiency diseases and cases associated with the toxicity of vitamins and minerals are of relatively low incidence, but other effects are probably of significant incidence. Generally, effects in this category can be described as occurring in a long-term basis, although acute toxic effects are also possible.

Environmental Contaminant Hazards

Among the plethora of chemicals to which humans are exposed, including those occurring naturally, the most important from a risk point of view are those classified herein as environmental contaminants. Included are the trace elements and organometallic compounds (e.g., arsenic, mercury, cadmium, tin, and lead), as well as a variety of organic substances [e.g., polychlorinated biphenyls (PCBs) and the halogenated hydrocarbon pesticides]. Although this category contains substances of quite diverse chemical structure, there are common characteristics in terms of behavior. The environmental contaminants tend to be stable and thus persistent in the environment, tend to bioaccumulate in the food chain, and can be biotransformed with increased toxicity. Illustrative reviews of the occurrence and the toxicity of the environmental contaminants (e.g., 46–48) indicate the importance of this class of compounds to food safety. Severity ranges over a wide spectrum of effects, depending on the duration and extent of exposure. Some of these substances (e.g., lead, mercury, and PCBs) have been shown to be of special concern in the case of the fetus, infants, and young children because of greater retention as well as susceptibility. The incidence of effects is difficult to quantitate for the environmental contaminants. By and large, incidence can be assessed only indirectly by combining what is known about toxicity with exposure data estimated by monitoring the levels found in food. Fortunately, regulatory controls in terms of permitted levels in foods appear from surveys to be helpful in minimizing human exposure, but unfortunately many consumers assume that since there is government approval, the affected foods are totally without hazard. Consistent with the spectrum of effects associated with these substances, the times of onset can vary widely from acute to long term. As noted, infants and young children are of special concern since effects induced in the short term [e.g., central nervous system (CNS) damage] can be of long-term significance.

Food Hazards of Natural Origin

The tens of thousands or perhaps even hundreds of thousands of compounds naturally present in foods could in part be incorporated with those of microbial origin and in part with the environmental contaminants. However, they are treated separately in this book because of their importance and need for attention in their own right. Only a small fraction of these substances have been identified, but among the known compounds are those with significant acute and chronic toxicity.

If one were to somehow solve all the scientific and public concern problems associated with substances directly or indirectly, deliberately or accidentally added to foods, there would still remain a set of food safety questions of immense magnitude and complexity—that of the natural contaminants. These compounds include a large class of substances occurring in foods of plant origin ranging from the oxalates in spinach, through the glycoalkaloids in the white potato to the mushroom poisons. Also included are the trace elements and the toxicologically important mycotoxins occurring in grains and other foods susceptible to mold growth, such as the aflatoxins, ochratoxin, patulin, zearalenone, and the tricothecene toxins. Other important contaminants of natural origin include the pyrrolizidine alkaloids and paralytic shellfish poison. In addition, a large set of coumpounds produced in foods during storage, processing, or preparation, such as the nitrosamines and polynuclear aromatic hydrocarbons, are included. Two articles by Hall (30, 49) provide an excellent overview of these substances, many of which have also been reviewed by the National Academy of Sciences (46).

These contaminants of natural origin are of importance not only because of direct human consumption, but also because of secondary exposure from the edible by-products of food-producing animals. In terms of severity, this class contains acute toxicants as well as potent carcinogens. The incidence of effects associated with these constituents cannot be well quantitated, but the case of aflatoxins presents one indication of the need for concern and the possible improvements that might result from control measures (50). In accord with the wide range of potential effects, onset can vary from acute to long term.

Food and Color Additive Hazards

If public attention were the criterion, food and color additives would rank highest. However, in terms of risk, they rank below the preceding categories (31–34). This class includes a wide variety of substances—over 2000 direct additives and perhaps on the order of 10,000 indirect additives, although most of the indirect additives probably do not actually end up in finished foods. By our definition of the category, it also includes several hundred drugs used in food-producing animals.

The discrepancy between public attention and inherent hazard is in large part due to a lack of understanding of the definition of the term "additive." Contrary to popular perception, the majority of direct food additives are GRAS substances. These substances, predominantly spices and flavors, include many familiar food ingredients, some of which, like salt and certain spices, have been used for thousands of years. Review of the safety information on certain GRAS substances has revealed that about 90% present no significant hazard with normal human food uses. Most of the remaining, although requiring adddditional testing to meet today's scientific standards, have not been associated with hazards to humans. The other direct additives used in foods have been approved, and their uses have been regulated by the FDA. Indirect additives, such as those used in production, processing, and packaging and that might migrate to food, are numerous but normally occur in foods, if at all, at trace levels—many at parts per billion or less. Examination of severity, incidence, and onset of effects for this very large class of constituents indicates the lowest-ranking hazard.

Regardless of the risk ranking of food additives, it is consistent with sound public policy to periodically review their safety, as well as to review other factors that affect food safety, in light of rapidly advancing science and changing food consumption patterns. This review of food additives, encompassing GRAS substances, direct and indirect food additives, color additives, and drugs used in food-producing animals, is now a standard activity of the Food and Drug Administration (51).

ASSESSING THE SAFETY OF FOOD COMPONENTS

Much of the confusion about the safety of our food supply and the relative risks associated with its various aspects derives from our inability to adequately measure the safety—or, more precisely, the risk—of food components. Whether it is a microbial toxin, an essential vitamin, a natural or other environmental contaminant, or a food additive, we would like to know what risk a given exposure presents (28). In some cases there is risk evidence from direct human experience or from epidemiology studies, but in most cases we are forced to rely on animal or other laboratory tests.

Although animal tests at high dose levels—perhaps a thousand times the equivalent of normal human exposure—are treated with public skepticism, the fear of another thalidomide lurks in the back of our minds. Then, too, if animal tests are to be discounted, what are we to conclude about the many substances whose use is based on an absence of adverse effects in animal tests? Rather than dismissing animal tests (or other laboratory tests) entirely or in contrast accepting their results blindly, they should be considered in perspective. Although the regulatory decision maker or the public policymaker would like yes–no answers from the scientist, such is not always possible; more often than not the scientific answer is "maybe."

There are many staunch defenders as well as critics of the Delaney Clause, which prohibits approval of any food or color additive, "found to induce cancer when ingested by man or animal . . . ." However, the issue is much broader than just the Delaney Clause; the FFD&C Act requires that an additive be "safe" under its conditions of use and the public expects constituents of food to be "safe" regardless of whether they are legally classified as food additives. In this context, "safe" involves not only cancer, but also any other toxic effect. However, having noted the impossibility of assuring absolute safety, the question really concerns the kinds and the levels of potential risk involved. That question, in turn, poses a host of other questions involving the chemical structure of the compound as well as its mutagenic behavior, its metabolism and biological activity, its acute toxicity, its reproductive and teratology effects, and in each case its dose–response characteristics. Finally, there is the question of how to extrapolate from the animal tests to humans. Obtaining sound data in each of these areas and integrating it to form a pattern that permits scientifically valid regulatory decisions is easier said than done. The Food Safety Council has proposed a decision-tree approach incorporating all these facets of toxicology and leading at several stages to a "pass," "fail," or "more testing" decision (28). Of course, a public-policy decision relative to a given food constituent may well weigh other considerations, and that possibility has generated a great deal of discussion relative to the risk–benefit concept (e.g., 52–56).

The preceding problems of safety or risk assessment are discussed in Chapter 7 with the objective of lending additional insight to the overall question of food safety. This final chapter, together with Chapters 2 through 6, should enable the reader to gain an overall perspective on food safety and thus place in proper context the continuing deluge of scientific and media reports on the safety of food constituents. The references in each chapter provide sources for the reader who is interested in pursuing these food safety topics in more depth.

REFERENCES

1. J. S. Turner, *The Chemical Feast: Ralph Nader's Study Group Report on the Food and Drug Administration*, Grossman, New York, 1970.
2. J. Verrett, *Eating May Be Hazardous to Your Health*, Simon and Schuster, New York, 1974.
3. E. M. Whalen and F. J. Stare, *Panic in the Pantry*, Atheneum, New York, 1973.
4. J. Hightower, *Eat Your Heart Out*, Crown, New York, 1975.
5. B. F. Feingold, *Why Your Child Is Hyperactive*, Random House, New York, 1975.
6. E. M. Whalen, *Preventing Cancer*, Norton, New York, 1977.
7. E. M. Whalen and F. J. Stare, *Eat OK, Feel OK: Food Facts and Your Health*, Christopher, North Quincy, Mass., 1978.
8. American Council on Science and Health, *Cancer in the United States: Is There an Epidemic?*, New York, 1978.
9. J. J. Fried, *The Vitamin Conspiracy*, Saturday Review Press, New York, 1975.
10. National Science Foundation, *Chemicals and Health*, U.S. Government Printing Office, Washington, D.C., 1966.
11. Editors, *FDA Consumer*, 13 (3), 2 (1979).
12. H. Tarnower and S. S. Baker, *The Complete Scarsdale Medical Diet*, Rawson, Wade, New York, 1979.
13. N. Pritkin and P. McGrady, Jr., *The Pritkin Program for Diet and Exercise*, Grossit and Dunlap, New York, 1979.

14. D. R. Reuben, *Everything You Always Wanted to Know About Nutrition*, Simon and Schuster, New York, 1978.
15. U.S. Senate Select Committee on Nutrition and Human Needs, *Dietary Goals for the United States*, U.S. Government Printing Office, Washington, D.C., 1977.
16. A. E. Harper, *Am. J. Clin. Nutr.*, 31, 310 (1978).
17. U.S. Senate Committee on Agriculture, Nutrition and Forestry, *Food Safety: Where Are We?*, U.S. Government Printing Office, Washington, D.C., 1979.
18. W. R. Barclay, *J. Am. Med. Assoc.* 242 (7), 657 (1979).
19. R. L. Hall, *Chem. Technol.*, 3 (7), 412 (1973).
20. R. Tannahill, *Food in History*, Stein and Day, New York, 1973.
21. E. Corwin, *FDA Consumer*, 10 (9), 10 (1976).
22. W. C. Frazier, *Food Microbiology*, 2nd ed., McGraw-Hill, New York, 1967.
23. H. W. Wiley, *An Autobiography*, Bobbs-Merrill, Indianapolis, 1930.
24. O. Anderson, *The Health of a Nation; Harvey Wiley and the Fight for Pure Food*, Univ. Chicago Press, 1958.
25. H. Hopkins, *FDA Consumer*, 10 (6), 10 (1976).
26. *Federal Food, Drug, and Cosmetic Act, as Amended*, U.S. Government Printing Office, Washington, D.C., 1979.
27. W. W. Lowrance, *Of Acceptable Risk*, William Kaufmann, Los Altos, California, 1976.
28. Food Safety Council, *Food Cosmet. Toxicol.*, 16, Suppl. 2 (1978).
29. H. R. Roberts, *Fed. Proc.*, 37 (12), 2575 (1978).
30. R. L. Hall, "Naturally Occurring Toxicants and Food Additives: Our Perception and Management of Risks," *Proceedings of Marabou Symposium on Food and Cancer*, Caslon Press, Stockholm, 1978, pp. 6–20.
31. V. O. Wodicka, "Food Safety in 1973," *Proceedings of Flavor and Extract Manufacturers Assoc.*, Washington, D.C., 1973.
32. R. L. Hall, *Nutr. Today*, 8 (4), 20 (1973).
33. A. M. Schmidt, *Address at Food Safety—A Centenary of Progress Symposium*, London, October 1975.
34. A. S. Truswell, N. G. Asp, W. P. T. James, and B. MacMahon, "Conclusions," *Proceedings of Marabou Symposium on Food and Cancer*, Caslon Press, Stockholm, 1978, pp. 112–113.
35. E. M. Foster, *Fed. Proc.*, 37 (12), 2577 (1978).
36. I. C. Munro and S. M. Charbonneau, *Fed. Proc.*, 37 (12), 2582 (1978).
37. J. V. Rodricks, *Fed. Proc.*, 37 (12), 2587 (1978).
38. J. Doull, *Fed. Proc.*, 37 (12), 2594 (1978).
39. National Academy of Sciences, *Prevention of Microbial and Parasitic Hazards Associated with Processed Foods*, Washington, D.C., 1975.
40. Staff Report, *Nutr. Today*, 10 (5, 6), 4 (1975).

41. T. Fodor, C. Reisberg, H. A. Hershey, and H. Berkowitz, *Public Health Rep.*, 85, 1013, (1970).

42. K. C. Hayes and D. M. Hegsted, "Toxicity of the Vitamins," in National Academy of Sciences, *Toxicants Occurring Naturally in Foods*, 2nd ed., Washington, D.C., 1973, pp. 235–253.

43. E. J. Underwood, "Trace Elements," in National Academy of Sciences, *Toxicants Occurring Naturally in Foods*, 2nd ed., Washington, D.C., 1973, pp. 43–87.

44. Food and Nutrition Board, *Recommended Dietary Allowances*, 9th ed., National Academy of Sciences, Washington, D.C., 1980.

45. Food and Drug Administration, *Fed. Reg.*, 43, 60883 (1978).

46. National Academy of Sciences, *Toxicants Occurring Naturally in Foods*, Washington D.C., 1973.

47. World Health Organization, *Environmental Health Criteria—2*, Geneva, 1976.

48. Office of Technology Assessment, *Environmental Contaminants in Food*, U.S. Government Printing Office, Washington D.C., 1979.

49. R. L. Hall, *Nutr. Today*, 12 (6), 1 (1977).

50. Food and Drug Administration, "Assessment of Estimated Risk Resulting from Aflatoxins in Consumer Peanut Products and Other Food Commodities," Washington, D.C., 1978.

51. H. Hopkins, *FDA Consumer*, 11 (5), 8 (1977).

52. P. B. Hutt, *Food Drug Cosmet. Law J.*, 33 (10), 505 (1978).

53. Expert Panel on Food Safety and Nutrition, Institute of Food Technologists, *The Risk/Benefit Concept as Applied to Food*, Chicago, 1978.

54. H. R. Roberts, *Food Technol.*, 32 (8), 59 (1978).

55. H. R. Roberts, *Food Drug Cosmet. Law J.*, 34 (3), 153 (1979).

56. *Principles and Processes for Making Food Safety Decisions*, Report of the Social and Economic Committee of the Food Safety Council, Washington, D.C., 1980.

CHAPTER 7

Food Safety and Toxicology

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Previous chapters in this book have examined five major areas that impact on food safety. These areas were assigned a relative ranking for hazards presented to humans on the basis of what is known and unknown (mostly the latter) about the risks involved in each case. As was noted, there is relatively little information derived from actual evidence of hazards to humans. Existing food safety data consist in part of isolated observations of acute effects arising from accidental exposures, some clinical information (e.g., therapeutic treatment with vitamins), and a limited number of epidemiology studies. For the most part, however, the inventory of toxicity data consists of results from animal studies. (Recently an increased amount of data from genetics toxicology testing is also beginning to become available.)

Because of the heavy dependence of our food safety knowledge on the results of animal toxicology, it is of value to examine this area to further assist in putting all aspects of food safety in proper perspective.

In the last 20 or even in the last 10 years, toxicology has advanced tremendously in importance and in application. Nonetheless, the conduct of animal toxicity tests and their evaluation is in a state of flux. Toxicology as a scientific discipline is under stress not only from the demands it is receiving for manpower and facilities, but also from external and internal criticism which is impacting on its credibility.

Growing concern and confusion about the safety of food additives and chemicals in our environment, together with what has been described as a national cancer phobia, have led to numerous reviews of safety for existing substances, testing of old and new substances, and the formulation of new controls on testing. Examples of the former include the FDA review of GRAS substances, the FDA cyclic review of direct and indirect food additives (see Chapter 6), the National Cancer

Institute's Carcinogenesis Testing Program and the National Toxicology Program. Examples of the latter include the many attempts at guidelines prescribing how to conduct and evaluate animal toxicity tests such as the efforts of the Interagency Regulatory Liaison Group (The Consumer Product Safety Commission, the EPA, the FDA, and the Occupational Safety and Health Administration). The Interagency Regulatory Liaison Group (IRLG) has published draft guidelines for several acute toxicity tests, including eye irritation; oral toxicity in rodents; dermal toxicity; inhalation in rats; and teratogenicity testing in rats, mice, and rabbits (1). Guidelines for chronic testing are also being developed by the IRLG. In a similar fashion, the United Kingdom has developed draft guidelines for the testing of chemicals for mutagenicity as well as carcinogenicity (2, 3), showing the international nature of such trends. The FDA has also promulgated Good Laboratory Practices (GLP) regulations (4) prescribing the conduct, monitoring, and reporting of animal studies.

The movement toward standardized testing is viewed by some with reservation, however. For example, the Select Committee on GRAS Substances (SCOGS) has cautioned against the development of rigidly standardized protocols for safety evaluation, noting that such an approach fails to recognize that all chemicals do not act in the same fashion. What is needed according to the SCOGS is a set of principles and guidelines that permit tailoring the tests to the particular nature and intended uses of the substance in question (5).

The current emphasis on toxicology has, in turn, led to a recognition of an insufficient number of toxicologists and testing facilities to do all the review, testing, and evaluation that might appear to be desirable. Efforts to define proper priority for attention such as that proposed by the Food Safety Council (6) have been a logical consequence of this recognition.

With respect to the training of new toxicologists and those in related disciplines, and with respect to increasing available testing facilities, the problem can be alleviated, at least in the long term, with proper attention and financial resources. However, a perhaps more worrisome concern is that of the credibility problem.

The public appears to have growing skepticism about the validity of animal tests that seem to produce a new carcinogen every week. This is especially the case when our diet foods and beverages; bacon, ham and sausage; and even our beer and scotch whiskey come under attack. The proposed banning of saccharin led to such a public rebellion that Congress interceded to delay any regulatory action. The anticipation of similar regulatory action in the case of nitrite brought pressure on the FDA to reevaluate the latest animal studies. At the same time there appears to be some concern that, if long-used substances are only now being associated with harm, there must be many other harmful substances that have not yet been identified. Finally, there is the lurking fear that if careful scientific scrutiny is not widely applied, there could be a thalidomide-type disaster.

In general, the response of the regulatory agencies has been toward stricter controls. As noted, for example, the FDA has put into effect its GLP regulations. Individual federal agencies and the IRLG are developing standardized testing guidelines and protocols for the whole range of toxicological tests. There are, however, also some signs of a tendency toward a more flexible regulatory policy. For example, the IRLG has issued a report addressing the question of risk assessment procedures (7). The natural consequence of stricter control has been the charge of bureaucratic red tape by some; and others in industry, the academia and Congress, are questioning what costs will be involved and what benefits will be derived from such trends.

SCIENCE AND PUBLIC POLICY

Although the scientific questions are difficult enough, the controversy relative to food safety also involves substantial questions of public policy. Even if the toxicologists could precisely determine the risk involved with a given food component, there would still remain the public policy question of how to regulate that component. Hutt (8), for example, has pointed out, in discussing the Delaney Clause, that the food safety controversy is in large part due to the failure to distinguish between the questions involving scientific determinations and those in which a public policy determination is required. By the same token, public policy and scientific determination each affect the other. The debate focusing on the Delaney Clause is a case in point. If a public policy determination is going to be made that the Delaney Clause should be retained as is, extended to effects other than cancer, revoked entirely, or modified in some way, that determination should be based on the best scientific information available.

The passage by Congress in 1958 of the Food Additives Amendment, including the Delaney Clause, to the FFD&C Act was an expression of both the public policy and the scientific knowledge of that time. Although there was debate about inclusion of the Delaney Clause, there was probably a consensus in its favor in 1958. Since then, however, its opponents have increased, as has the level of debate. In 1962 a modified Delaney Clause was incorporated into the FFD&C Act to permit the use of a carcinogenic drug or feed additive in food-producing animals, provided that no residue of such substance would be detectable in edible portions of the food animal. Perhaps this modification was a conscious reflection of a public policy changing to reflect scientific practicality, or perhaps it was only a somewhat clearer statement of the original intent. In any event, the regulatory implementation of a definition of detectability is still to be accomplished, and the Delaney Clause has remained unchanged.

The advances of science since 1958 have had a significant impact on the debate over public policy for food safety. This is especially true relative to analytical methodology. The IFT Expert Panel on Food Safety and Nutrition has noted that "At this point the ability of scientists to detect minute quantities of chemicals has outstripped their ability to interpret the findings" (9). Using DES as an example, the panel cites the current sensitivity of detection as 2 ppb and in some cases in parts per trillion—an increase in sensitivity about fiftyfold or more since 1958. A maximum of 2 ppb in liver compares to 4000 ppb DES equivalent in wheat germ, 1500 ppb in wheat bran, 2200 ppb in soybean oil, and 1800 ppb in peanut oil. On the order of 2500 to 25,000 times as much estrogenic activity occurs naturally in a 120-pound woman as would result from the average daily ingestion of liver containing 2 ppb of DES (9).

In addition to advances in analytical chemistry, toxicology testing has expanded with two-generation *in utero* exposure at maximum tolerated doses becoming the norm in chronic testing and more detailed histopathology becoming customary. Thus scientific knowledge of adverse effects is increasing, posing additional questions in the public policy arena.

It is certainly in order to separate, to the extent possible, scientific determination and public policy, but if food safety is to be better understood, more than that separation is required. We need to recognize that toxicity tests do not always provide answers to the public policy questions that are asked. That point can be explored, and at the same time the role of toxicology in food safety can be put in perspective by exploring three areas: the yes–no toxicology question, toxicity versus safety testing, and animal-to-human extrapolation.

YES–NO TOXICOLOGY QUESTIONS

There is a natural tendency on the part of the public and a growing tendency on the part of regulatory officials to demand yes or no answers to questions about the safety of food constituents—is it safe or is it not? As the reader has seen previously in this book, the answer to the question "Is substance X toxic?" must be "yes," since all substances have some toxic effects under some conditions of exposure (even the essential nutrients discussed in Chapter 3). As Paracelsus, a Swiss alchemist and physician (and recently the patron saint of toxicology), noted nearly 500 years ago, "All things are poisons, for there is nothing without poisonous qualities. It is only the dose which makes a thing a poison," (Paracelsus presumably spoke from first-hand experience since he is credited with making mercury, lead, and arsenic a part of the pharmacopoeia.) Thus no toxicological testing is necessary to answer such a question; the answer is "yes" to begin with.

The Delaney Clause (and indeed the basic safety requirements of the FFD&C Act with respect to food additives) asks the yes–no question with respect to carcinogenesis, "Is the substance a carcinogen (in humans or animals) or is it not?" No consideration is given to what is meant by the term "carcinogen," to the type of tumor involved, or to the relative potency of the compound. Neither is consideration given to the dose levels entailed, the frequency, and the route of exposure or other factors routinely involved in toxicological evaluation. All these excluded facets are of fundamental importance to toxicological evaluation. For example, Kolbye (10) has explained the wide variety of situations encompassed in the general term "carcinogen" and the need to make scientific and regulatory distinctions. Numerous other difficulties with the yes–no approach such as a compound metabolized to carcinogenic form in an animal species but not in humans can be determined without too much thought.

The yes–no philosophy, if extended, could lead to automatic disapproval of almost any substance considered. If the yes–no approach to carcinogenesis is logical, the next biological step might be mutagenesis (Is the compound mutagenic in any test at any test level?), then reproductive and teratological effects, then effects on any specific organ, and so forth.

There is a danger that the yes–no approach can adversely impact on rational assessment of food safety in other areas such as the trend toward standardized protocols and regulations for the conduct of animal studies. This potential is illustrated by the possibility that a negative study, departing in any regard from a rigid checklist, would be unacceptable for regulatory purposes, yet a study indicating positive effects, no matter how many departures from sound toxicology were involved, would classify the substance as unsafe. There are two major problems with these trends: they can lead to unnecessary studies, diverting scarce resources from higher priority problems, and they in no way assure that the right questions are asked on a case-by-case basis about the particular substance involved. We would do well to remember the admonition of the National Academy of Sciences:

> There is no substitute for the vigilance of an inquiring and skeptical mind which has assumed the full responsibility for planning, conducting and evaluating the results of toxicity tests in making safety assessments. If that responsibility is lessened by an exclusive dependence on a "checklist" approach, the major assurance has been lost that a responsible, perceptive and efficient investigation will be conducted (11).

The trend of the regulatory agencies to rely more and more on the "checklist" approach rather than what might be called *toxicological evaluation* is understandable. The FDA operates under a basic law that in many respects is inflexible. Then, too, the checklist approach makes the regulatory job much easier and removes the necessity to utilize and justify the scientific judgment that would otherwise be required. Finally, this approach appeals to the legal mind. Since many or even most of the difficult questions are ultimately decided by the courts, the yes–no answer is much more likely to be sustained on the basis of the record than is the scientific answer, which probably is "maybe." Although the black or white classification of answers is a regulatory convenience, toxicological problems like most other aspects of life come only in various shades of gray.

The public policy question involved in all of this is fundamentally whether, as a society, we want the regulatory agencies to rely on the yes–no approach. If that is the case, then we should embrace the Delaney Clause and the food additive safety provisions of the FFD&C Act and extend them to all toxic effects that might be associated with food and indeed beyond food to other environmental effects. It should be realized, however, that extension of the yes–no approach can ultimately lead only to disapproval of the entire food supply, for as we have seen in the previous six chapters, absolute food safety is impossible.

If, instead, the public policy question is resolved in favor of making scientific judgment an essential part of the safety decision process, there is hope. However, that path is not without difficulties. Quality toxicity testing will be required, but some flexibility must be built into the protocols and into the conduct, reporting, and evaluation rules. Further, there must be recognition of the fact that toxicology is a developing science. Therefore, differentiation must be allowed between accepted, standard techniques and those that are still research techniques. Information from both areas can and should be considered, but the flexibility to attach proper weighting to each must be permitted.

TOXICITY VERSUS SAFETY TESTING

The considerations involved in the safety assessment of food additives have been discussed in some detail in both Chapter 5 and Chapter 6 and are not repeated here. However, to understand food safety and the role of toxicology in its evaluation, a careful distinction must be made between toxicity testing and safety testing. To the toxicologists, toxicity is defined as the inherent ability of a substance to produce injury or adverse effects. Toxicity tests are carried out first to (*a*) identify what those adverse effects are and (*b*) determine the extent to which those effects occur as a function of dose. The basic purpose of the toxicity tests, then, is to find out what adverse effects the test substance produces regardless of the frequency, type, or level of exposure and to determine the dose-response characteristics of the substance relative to those effects. To elicit these answers, dose levels that are unrealistic in terms of human exposure will likely have to be utilized. Such dose levels, in fact, may be so high that the effects evidenced are due to some secondary mechanism rather than primary toxicity. A test substance cannot be characterized relative to toxicity without employing exposure conditions severe enough to produce the inherent toxic effects and to indicate the dose-response relationship involved.

Although the fact that the dose levels employed for toxicity evaluation may be unrealistically high in terms of human exposure is irrelevant to the toxicity question, it is highly relevant to the safety question. Recalling that absolute safety is impossible to demonstrate, safety can be defined as the probability that injury or other adverse effects will not occur from exposure to the test substance at a particular dose level and under specified conditions. It is, therefore, entirely possible to conduct an animal study that will answer the safety question for some particular exposure conditions but will give no information concerning the inherent toxicity of the test substance. Conversely, of course, a toxicity study can provide rather complete information about toxic effects but cannot answer the safety question unless there is also information about actual human exposure.

The distinction between toxicity testing and safety evaluation is not well understood, but the results of such toxicological thinking have been generally accepted in a public policy sense for the control of food safety. The exception to that statement is the case in which the toxic end-point is cancer. A separate treatment of the cancer situation, mandated by law (the Delaney Clause) has generated a wide investigation of and debate about the applicability of animal toxicity tests and how the results of such tests should be used for safety evaluation.

ANIMAL-TO-HUMAN EXTRAPOLATION

The information that we have on the toxicity of various components of our food supply has been derived mainly from animal tests, usually with rats and mice. This is especially the case relative to carcinogenesis testing, although in recent years an extensive body of information from a variety of genetics toxicology testing has also been generated. Public skepticism about the relevance to humans of animal tests conducted at dose levels much higher than human consumption levels has been widespread. The two basic questions in this regard relate to whether animal toxicity tests are appropriate for predicting hazards to man and, if so, how the extrapolation should be made.

The Animal Model for Toxicity

The question as to the appropriateness of animal toxicity tests must be answered with a qualified "yes." Toxicologists are generally committed to the belief that the effects observed in properly conducted animal tests, when suitably interpreted, are applicable to humans and that such tests represent the best currently available approach to the problem without actually doing the testing in humans. For example, the Office of Technology Assessment (12) strongly endorses the animal approach for carcinogenicity testing:

> Animal tests are the best current method for predicting the carcinogenic effect of substances in humans. All substances demonstrated to be carcinogenic in animals are regarded as potential human carcinogens; no clear distinctions exist between those that cause cancer in laboratory animals and those that cause it in humans. The empirical evidence overwhelmingly supports this hypothesis.

Some of the advantages of animal testing include the capability of studying a wide variety of effects, ranging from acute toxicity to long-term effects such as cancer, under controlled conditions. Effects on reproduction and offspring can also be studied. By sacrificing animals during the course of a study, the time dependence of an effect can be evaluated. In each case one or more routes of administration (e.g., in food, in drinking water, or by injection) can be used to mimic the manner in which human exposure occurs. A principal advantage of animal tests is time; normal life spans and gestation periods for rats and mice, for example, permit the assessment of reproductive effects, birth defects, and even chronic effects within a 2- to 3-year period.

The high doses utilized in animal studies are perhaps both advantageous and disadvantageous. Characteristically, we expect that the higher the dose, the greater the response. A dose that produces a response of, say, only 10% would not likely produce observed effects in an animal experiment, yet such a level of response occurring in the total U.S. population would be of serious consequence. The possibility of overlooking such a response is compensated for by testing at doses as high as possible, thus greatly increasing the likelihood of observing the effect. The disadvantage of that approach is that we gain no quantitative information about the dose-response behavior in the low-dose range (which probably corresponds to human exposure levels). In addition, care must be exercised in selecting the dose levels to be tested so that the results will be meaningful. This involves using, at most, the so-called maximum tolerated dose (MTD), that is, the highest dose that will not significantly affect survival or longevity or produce other toxicity in the test animals (13). (There is disagreement among toxicologists as to the MTD definition; arguments are advanced that in some animal testing the doses have been so high that they may have disrupted the normal physiology of the animal.)

There are several limitations to the use of animals for predicting toxicity in humans. Primary among these are the differences in kinetics between a given test species and humans, including differences in absorption, distribution, metabolism, and excretion. Further, the type of end-point and/or the target organ(s) may differ between animals and humans. Certain toxic effects such as those involving learning and behavior are at best quite difficult to assess, although this area is receiving increased emphasis, and the speciality of behavioral toxicology is coming into being (14, 15).

Generally speaking, mammals metabolize most of the compounds they ingest in similar fashion, but there can be pronounced differences between species. Such differences also occur with respect to other aspects of the kinetics involved. Therefore, the toxicologist attempts to select an animal model that handles the compound in similar fashion, if that is possible, and/or utilizes more than one species to increase the likelihood of detecting adverse effects. Of course, practical constraints of time, cost, and logistics have led to the popularity of rats and mice as the animal models.

Toxicity tests that are inappropriate for predicting the existence of a potential hazard in humans can produce either false negatives or false positives. Testing in more than one species helps to reduce the likelihood of both of these errors. However, regulatory toxicologists in particular must be more concerned about false negatives and, therefore, concentrate on that error, attempting to find the most sensitive species.

Specifically, with respect to cancer it is worth noting that virtually every form of human cancer has an experimental counterpart in animals and that every form of multicellular organism is subject to cancer, including plants, insects, and fish. There are, in fact, striking similarities between cancer in humans and in test animal species. Of course, there are differences, sometimes pronounced, in susceptibility between species, strains, and individuals for cancer, just as for other toxic effects. Therefore, especially with quantitative prediction, the same limitations and cautions apply to the cancer end-point as to any other toxic end-point.

In short, test animals can be useful models for predicting potential hazards in humans. The limitations associated with such models must be given careful consideration, however, in evaluating the potential human toxicity of a test substance. This requires maximum input by the toxicologist in the planning, execution, and evaluation of safety studies. Even the most detailed and comprehensive guidelines or legislative pronouncements are no substitute for the expertise provided by the experienced toxicologist. Then, too, it is critical that all existing information be utilized in making a safety evaluation. This should include the nature of the test compound (16) and its metabolism and kinetics in the different test species and in humans. Not only positive but also negative testing results should be considered, along with any auxiliary information, such as epidemiology studies, if they are available, and the results from genetics testing.

Risk Assessment Techniques

As noted previously, risk information relative to a given food constituent is usually available only in the form of animal or other laboratory test data. Usually, too, the response data are associated with dose levels several times in excess of normal human exposure. The problem is to infer what risk the food constituent presents to humans. Traditionally, the dose-response data obtained from the animal toxicity tests have been used to predict safe levels for humans. A threshold or a no-effect level (i.e., the dose that produces either no effect or for which the response is not different from that of the untreated control group) for the toxic effect under consideration is estimated from the animal data and then divided by a safety factor to obtain a safe level for humans.

Usually a safety factor of 100 is used to reflect both animal variability (by a factor of 10) and the potential difference in susceptibility between animals and humans (by a factor of 10). In some cases where human toxicity information is available a safety factor as low as 10 has been employed, and safety factors as high as 1000 or 2000 have also been used (e.g., for certain animal drugs) when there is uncertainty and concern about the toxic effect involved. Often further calculations are made to establish an ADI of the substance in question.

A safety factor of 100, or some other value, is admittedly somewhat arbitrary but can be in part justified by the noted animal variability in response and the potential for greater susceptibility in humans. Further, experience would indicate that the use of such a safety factor in the regulation of drugs, food additives, pesticides, and other chemicals to which humans are exposed has worked well over the years. However, when the toxic end-point of interest is cancer, the law (the Delaney Clause) proscribes the use of a safety factor in the case of a food or color additive or a drug used in a food-producing animal. (See Chapter 6 for a description of the legal aspects of these substances.)

The concept embodied in the Delaney Clause is that cancer-producing agents do not have a threshold or a no-effect level; however small the dose, there will be some response, and hence no carcinogen, regardless of its potency, is to be allowed. This aspect of the Delaney approach to safety evaluation is much criticized since the dose-response behavior of a substance is of fundamental importance in not only toxicology, but all biology including medicine. There is little, if any, argument in the case of carcinogens about whether they exhibit a dose-dependent response, since clearly they do. However, there is argument about whether some or all carcinogens have a threshold or a no-effect dose level at some point on the dose–response curve. Advocates of the no-threshold concept point out that the existence of a threshold has not been experimentally shown for any carcinogen. Their argument is obviously irrefutable since it is impossible to prove a negative. The absence of observed effects in even a very large number of animals proves only that there is at most a low degree of probability of effects in the total population.

The question of the existence of a threshold for carcinogens is an obviously important point with respect to food safety, since in safety evaluation it is generally the estimated no-effect level that determines the tolerance or other regulatory limit on the use of the test substance. As the argument about the existence of a threshold for carcinogens is incapable of absolute resolution, it will likely continue. In the meantime, it is clear that most toxicologists believe that even though there may not be a true threshold, there is, indeed, an effective or practical threshold for many carcinogens, with a response sufficiently low to be of no toxicological significance. Such practical thresholds can well be accepted as existing if one acknowledges the body's normal detoxification and repair mechanisms. Accepting the existence of effective thresholds then logically leads to the reasoning, advanced by many, that carcinogens should be regulated on a case-by-case basis, taking into account the observed dose–response evidence. In this way the same ground rules that are applied elsewhere in toxicology could be applied to carcinogens, thus permitting differentiation among carcinogens on the basis of potency rather than relying on the legislative approach of the Delaney Clause, which permits no differentiation.

The Delaney Clause has prompted a great amount of scientific and public-policy debate over its attributes and shortcomings. Along with the debate, a great deal of attention has been devoted to mathematical techniques for extrapolating observed animal dose–response data to provide estimates of the risk to humans, usually at dose levels much below those to which the animals have been exposed. The appeal of such risk estimation is that it avoids the classification of a substance as safe or unsafe and also avoids the necessity of entering the debate about thresholds. If some acceptably small level of risk is selected (that level must be a societal decision), the extrapolation techniques can be used to establish the corresponding dosage levels.

A detailed treatment of mathematical techniques for risk extrapolation is beyond the scope of this book, but a brief summary will assist the present discussion. It should first be noted that these extrapolation techniques have, for the most part, been applied only to carcinogenesis risk estimation. The Food Safety Council (6), however, has pointed out that an extrapolation model that encompasses a variety of forms for the theoretical dose-response function can be applied to any end-point whether it is from acute or chronic testing or from mutagenic or teratology studies. Roberts (17) has gone a step farther by advocating the replacement of safety factors with extrapolation techniques, arguing that "There is as little justification for the assumption that a non-carcinogenic response always has a threshold as there is for the assumption that a carcinogenic response never has a threshold."

There are various mathematical models that have been applied to the risk assessment problem. These have been reviewed by the Food Safety Council (6) and Roberts (17), among others. (The interested reader is referred to those reviews and to the references following for more detail.) The two most popular extrapolation models have been the Mantel–Bryan Model (18, 19) and the so-called one-hit model (20). Both have primarily been applied to carcinogenic risk estimation. Other major models include the Armitage–Doll multistage model (21), the Cornfield pharmacokinetic model (22), and the gamma multihit model (23); the last was recommended by the Food Safety Council. In addition, mathematical models (24, 25) have been proposed for risk extrapolation which are based on the time to response. Generally, however, response time data are not available from toxicity studies.

It is difficult at best to argue in favor of any one of these models over any other. As noted by Cornfield (22), all such models are subject to major shortcomings:

- The choice of model drastically affects the calculated dose corresponding to an acceptable risk level, several orders of magnitude in some cases.
- Observed dose response data can often be fitted equally well by any of the models, providing no obvious statistical basis for response behavior in the low-dose range.
- No firm scientific basis now exists for choosing among alternative extrapolation techniques.

Nonetheless, the use of such techniques in the case of carcinogenesis permits the evaluator to rank the substances involved in terms of their potential hazard and to make a priority assessment relative to control actions. For example, application of any of these techniques—even accepting the dose-response data at face value—would show that any cancer risk associated with saccharin is at worst several orders of magnitude less than that for aflatoxin or dimethylnitrosamine (6).

In a discussion of extrapolation methods prepared for the Office of Technology Assessment, Crump and Masterman (26) caution that the selected method should, to the extent possible, reflect the known or plausible information relative to the biological mechanisms involved. For example, these authors point out the theoretical arguments for treating "directly acting carcinogens" that have been advanced by several writers (27–29). The "directly acting carcinogens" are those for which either the agent itself or a metabolite acts at the cellular level to produce a heritable change that eventually leads to tumor formation. In such cases, and in others where the agent adds to an ongoing background process of tumor formation, the argument can be made that the dose–response function is linear at low doses (i.e., has a positive slope) (30). Because of the theoretical arguments that can be advanced for low-dose linearity of the dose–response function and the conservatism (relative to risk estimation) that is entailed, many scientists advocate extrapolation méthods encompassing low-dose linearity unless it can be ruled out on the basis of knowledge of the mechanism involved.

Until we increase our present knowledge about the mechanisms involved in cancer, it will not be possible to utilize extrapolation models with certainty. However, these approaches are finding increasing use in the regulatory arena [e.g., the FDA proposal relative to animal drugs (31) that entails the one-hit model] and lend support to the valid need for relative risk assessment in food safety.

FOOD SAFETY REGULATION

Recognizing that we are only deluding ourselves when we seek the noble goal of absolute food safety—for such is not possible—what should be the basis for food safety regulation? This question is normally addressed in terms of the controversial Delaney Clause.

There are probably four options currently possible for dealing with the Delaney Clause. The first is to leave it as it is. That would satisfy relatively few and would maintain the current confusion and concern. A second approach would be to extend its coverage. This would satisfy even fewer of us and would multiply the confusion and concern, but this seems to be the direction in which we are heading. A third approach would be to simply eliminate it. That approach probably has more supporters than either of the first two approaches. However, it is not likely to happen, and even if the Delaney Clause were eliminated, the basic safety provisions of the FFD&C Act could leave us on the horns of the same regulatory dilemma. Thus we are left with the fourth approach, which is to modify the Delaney Clause in some fashion. Many different versions of this approach have been advocated.

The toxicologists have developed one collective version of a modified Delaney Clause. The Society of Toxicology Technical Committee has suggested the following wording:

> No additive shall be deemed free of risk of inducing human cancer if it is found to induce cancer when ingested by man or if it is found, after tests which are appropriate for the evaluation of the health risk of food additives, to induce cancer in animal species that metabolize the additive in a manner similar to man.

This version contains the two important aspects of metabolism and risk assessment, both of which are basic to the restoration of scientific judgment to the regulation of food safety.

Lowrance (32) has suggested that safety should be redefined as a judgment of the acceptability of risk. That suggestion has a good deal of merit, for it is only in this way that public policy will be able to keep pace with the advancing frontiers of science. The advantage of treating carcinogens from the risk assessment point of view is that it recognizes the irrefutable scientific fact that not all carcinogens are alike. Some carcinogens are much more likely to produce human cancer, and not all human cancers are alike. If risk assessment were inserted into the regulatory process, there would be a quantitative mechanism for evaluating carcinogens individually rather than as a group.

The General Food Safety Issue

In addition to the specific issue of the Delaney Clause, the broader issue of food safety has also been widely debated. For example, the regulators themselves have addressed food safety. Miller (33) has stated that a regulatory system should (*a*) establish categories of risk (i.e., unavoidable contaminants, food and color additives, spices and herbs, nutrients, etc.), (*b*) be flexible enough to permit a reasoned response, (*c*) allow, when possible, a variety of regulatory options, and (*d*) encourage the development of the safest possible food supply. However, Miller also cautions that:

> if we are to move to a New Evangelism based upon the recognition of relative risks, then it must also be an Informed Evangelism founded upon sound data which reveal the nature and extent of the hazards to which we are exposed.

A wide range of ideas have been expressed by the legislators. It is interesting to note that one of the few congressmen with scientific training (organic chemistry), Representative James G. Martin, introduced a bill, H.R. 5091, in the 96th Congress to modify food safety assessment. This bill 5091 would permit approval of a food additive if:

> based on all the data presented the benefit from the reasonable anticipated use of the food additive by the persons who can reasonably be expected to use the additive outweighs the risk to such persons from

> such use, or that the risk to humans, as extrapolated to humans from test data on animals by normal statistical methods, is so low as to be clearly acceptable in the context of overall safety and reliability of the food supply.

This bill also addresses risk assessment and the use of the maximum tolerated dose concept in evaluating animal carcinogenic studies.

In response to requirements of the Saccharin Study and Labeling Act, the National Academy of Sciences examined food safety policy and issued a report containing a number of recommendations (34). These recommendations were that a new food safety system should be established with the basic features of comprehensiveness, discrimination among risk levels, flexibility in response, education, regulatory discretion, and accountability and jurisdiction. Basically, the academy recommended that there should be a single standard for the safety of all components of food. This standard should encompass four categories of risk (high, moderate, low, and none) with flexible regulatory options for each category. (The "none" category would cover those substances showing no evidence of hazard or presumed safe on the basis of use experience.)

The range of views on the complex subject of food safety regulation are illustrated by the papers presented at the 1979 Symposium of the Institute of Food Technologists on Developing Public Policy for Food Safety (33, 35–40). Despite the divergence of views, however, all these authors espouse the importance of science and risk evaluation in food safety policy decisions.

In many aspects of life we at least subconsciously recognize that risks are involved and also make decisions about our activities based on the degree of associated risk. Hutt (41) has summarized the annual risk of death for several common activities, and some of these are illustrated in Table 7.1. The data in Table 7.1 indicate the fact that no aspect of life is free of risk. However, the risks associated with food are not as obvious as the examples cited. We have seen in previous chapters that deaths associated with foods are the exception rather than the rule. We have also seen that the more subtle toxic effects attributed to foods, although present naturally as well as because of the actions of humans, are difficult to quantitate. Nonetheless, by considering what is known and what can be determined about food risks, food safety can be put in proper perspective and meaningful priorities for attention can be assigned.

A New Food Safety Policy

The continuing efforts of government and industry to not only keep food risks at a minimum, but to further decrease those risks would be materially aided by a national food safety policy which set priorities

TABLE 7.1 Annual Risk of Death Associated with Common Activities in the United States

Type of Activity	Risk of Death Per Year Per 100,000 Population
Motor Vehicles	22.0 (1/4,550)
Home Accidents	1.2 (1/83,330)
Alcohol (cirrhosis-1974)	16.0 (1/6,250)
Air travel (one transcontinental trip per year) (1974)	0.3 (1/333,330)
Amateur Boxing (40 hours/year)	2.1 (1/47,620)
Skiing (40 hours/year)	3.0 (1/33,330)
Canoeing (40 hours/year)	40.0 (1/2,500)
Rock Climbing (40 hours/year)	100.0 (1/1,000)
Fishing (drowning)	1.0 (1/100,000)
Recreational (drowning)	1.9 (1/52,630)
Bicycling	1.0 (1/100,000)
Occupational	
Airline Pilot	30.0 (1/3,330)
Truck Driver	10.0 (1/10,000)
Fire Fighter (1971-72)	80.0 (1/1,250)
Coal Miner (1970-74)	130.0 (1/770)

[a] Based on 1975 data except as noted.

Source. P. B. Hutt, Food Drug Cosm. Law J.. 33 (10), 558 (1978).

based on the risks rather than the politics and the emotion involved. Such a policy sould contain the elements of:

- Comprehensiveness
- Consistency
- Flexibility
- Peer review
- Public participation
- Education

It is critical that our national food safety policy encompass all areas of potential hazards, including those of microbiological, nutritional, environmental, natural, and food additive origin discussed in this book. To do otherwise is at best a waste of scarce scientific resources and at worst a jeopardy to our health. We must consider hazards of natural as well as man-made origin and direct our efforts in the priority areas dictated by the risks to humans. Further, we have seen in previous chapters the very large extent to which individual food-related problems can interact with one another. Thus only a comprehensive approach can be truly effective in maintaining and improving food safety.

Consistency must also be a keystone of food safety policy. This does not imply a rigid checklist or a yes–no approach, but rather a general framework permitting the treatment of individual problems on a case-by-case basis. That framework should apply whether the origin of the problem is man-made or due to nature, or both. The basis for consistent treatment must be the evaluation of risk. As noted in the preceding, such evaluation would entail identification of the type, the extent, and the onset time of adverse effects; species-to-species variability in susceptibility; differences in metabolism and kinetics among test species and humans; dose–response characteristics; and human exposure, including any particularly vulnerable subpopulations. The subsequent regulatory mechanism selected should be aimed at reducing the risks involved, again regardless of whether the origin of the problem is humans or nature (41). However, the regulatory control imposed must be consistent with the additional practicalities involved in each particular case.

Maintenance and improvement of food safety also requires flexibility in regulatory policy (and hence in the law that provides the basis for that policy). There must be sufficient latitude in the regulatory process to maintain consistency yet still permit the tailoring of regulatory controls to the individual situation. Different components of food involving the same type and level of risk should not necessarily be regulated in exactly the same way unless the risk is so great as to warrant rigid control or so minimal as to warrant little or no control. Although reduction of risk should always be the regulatory objective, the means of achieving that objective will differ and will likely involve different economic, health, and other factors depending on the food constituent involved. Unless precluded by an obviously high level of risk, which is rare in food safety, the ultimate regulatory control thus should take into account the impacts on health and on the nutritional value, the availability, the acceptability, and the consumer cost of foods. Such flexibility in regulatory policy could reduce risks across the board without unduly impacting on the food supply. In addition, it would leave open the possibility of informative labeling of certain foods or other means of conveying consumer information, thus preserving freedom of choice in the marketplace. Such labeling or other information must, however, be considerably improved over the simple and misleading kind of dire warning utilized in the case of saccharin (41). Probably the best reason for permitting, or better yet, directing, flexibility in regulatory control of food safety is the reminder of the Food Safety Council:

> The purpose of regulation should be to serve the best interests of the consumer and neither to be subservient to the producer nor to dictate to the consumer. In our current system there are many instances of arbitrary restriction on freedom of choice (42).

If we are to restore some measure of public credibility to scientists and especially regulatory scientists, peer review must play a greater role in food safety decisions. Such review in other than routine decisions could assist measurably in improving overall food safety and could greatly augment the scientific expertise available to regulatory agencies. Subsequent to an evaluation of the risks involved in a given situation, the regulatory agency(ies) involved should have the prerogative to convene an appropriate expert panel to review that evaluation. (The emphasis should be on "appropriate" and on "expert." Members should be recognized authorities in the particular areas involved and not merely self-appointed "experts.") By the same token, parties that could be affected by a subsequent regulatory decision should have the right to request and, having shown cause, be granted the formation of such an expert panel. The one caveat to the inclusion of peer review in the regulatory process is the obvious requirement of a regulatory agency to deal with emergency situations. In emergency situations requiring immediate actions, temporary controls could be invoked, to be reviewed subsequently by an expert panel and then modified as necessary. It is also important that the findings of an expert panel be made public in sufficient detail to permit public understanding of the issues involved.

Public participation has become an integral part of regulatory rulemaking. It should remain a part of any new food policy and should be incorporated into any new food law. Information gathered by a regulatory agency relative to a given food component or food problem should be made public, and comment should be invited prior to any agency action. As noted, this would include the findings of any expert panel involved in the issue. In the event of emergency, the immediate action taken should be explained to the public as soon as possible. Any subsequent modifications to the initial approach should also be made public. The information made public should include details on the types of risks and their potential extent in humans and possible regulatory options. For the options cited, the impacts should be identified, including any reduction in risks and effects on consumer costs, availability, and acceptability of foods, nutrient values, and any health-related effects. Such information must be balanced and complete, however. Negative as well as positive effects observed in animal tests, any available epidemiology or other auxiliary information, exposure data, and so on, must all be presented to present a useful explanation to the public.

The final piece in the puzzle of a new food safety policy, and in many ways the most important, is that of education. Consumers are beginning to realize that absolute food safety is impossible and are showing some willingness to weigh the risks in a given situation against what they perceive to be benefits and to act accordingly. However, few consumers have even a basic understanding of animal testing or its role in predicting human hazard. Perhaps fewer still are aware of the importance of microbiological hazards, realize that essential nutrients can be toxic, or recognize that naturally occurring foods contain toxicants. Many consumers are not aware of the fact that our life spans are increasing and that the death rates of major diseases such as heart disease and many forms of cancer are decreasing. Industry, government, and academia have collectively done a poor job of conveying to consumers the admittedly complex facets of food safety! Thus much of the public's "education" in this regard has been left to alarmists, attention seekers, and purveyors of worthless (and sometimes dangerous) health products. For public acceptance and success, any new food safety policy must encompass a mechanism for first explaining the basics of food safety to consumers. There must also be a built-in mechanism for explaining the facts of a food-related problem and the reasons for adopting a particular regulatory course of action. Accomplishing these education needs will by no means be an easy task, but with a dedication to that end incorporated into a new food safety policy, it can be done.

CONCLUSION

Although many food professionals agree on the need for a new food safety policy and even agree on many of its components, such change will be slow in arriving. Modernization of the Delaney Clause and associated food safety demonstration requirements to get past the most visible current issues could be accomplished with only minor modifications of the FFD&C Act, but even this is not likely to happen quickly. Revision of food safety law to incorporate consistent risk evaluation and permit regulatory flexibility would require considerable modification of nearly all sections of the Act as well as modifications of associated food laws. New public policy of this nature is always slow in evolving.

Despite the difficulties of achieving it, new food safety policy is critically needed and must continue to be sought after by Congress, regulatory agencies, industry, academia, professional societies, and public interest groups. All these groups must explain to the public that we cannot guarantee a risk-free society, and this pertains to food as well as other aspects of life. We must painstakingly strive to present to the public in understandable terms the whole complex story of food safety, instead of taking the easy way out—the oversimplified but alarming and confusing statement on each new food safety issue. It is only by this route that consumers will come to understand the issues and accept the fundamental changes that need to be accomplished.

REFERENCES

1. Interagency Regulatory Liaison Group, *Draft I. R. L. G. Guidelines for Selected Acute Toxicity Tests*, Environmental Protection Agency, Washington, D.C., 1979.
2. United Kingdom Department of Health and Social Security, *A Consultative Document on Guidelines for the Testing of Chemicals for Carcinogenicity*, London, 1979.
3. United Kingdom Department of Health and Social Security, *A Consultative Document on Guidelines for the Testing of Chemicals for Mutagenicity*, London, 1979.
4. Food and Drug Administration, *Fed. Reg.*, 43, 59986 (1978).
5. Select Committee on GRAS Substances, *Fed. Proc.*, 36 (11), 2519 (1977).
6. Food Safety Council, *Food Cosmet. Toxicol.*, 16, Suppl. 2 (1978).
7. Interagency Regulatory Liaison Group, *Fed. Reg.*, 44, 39858 (1979).
8. P. B. Hutt, *Food Drug Cosmet. Law J.*, 33 (10), 541 (1978).
9. IFT Expert Panel on Food Safety and Nutrition, *The Risk/Benefit Concept as Applied to Food*, Institute of Food Technologists, Chicago, 1978.
10. A. C. Kolbye, Jr., *Proceedings of the Third Annual Meeting, The Toxicology Forum*, 84, Washington, D.C., 1979.
11. National Academy of Sciences, *Principles for Evaluating Chemicals in the Environment*, Washington, D.C., 1975.

12. Office of Technology Assessment, *Cancer Testing Technology and Saccharin*, U.S. Government Printing Office, Washington, D.C., 1977.
13. I. C. Munro, *J. Environ. Pathol. Toxicol.*, 1, 183 (1977).
14. C. V. Vorhees, R. E. Butcher, R. L. Brunner, and T. J. Sobotka, *Toxicol. Appl. Pharmacol.*, 50, 267 (1979).
15. R. L. Brunner, C. V. Vorhees, L. Kinney, and R. E. Butcher, *Neurobehav. Toxicol.*, 1, 79 (1979).
16. G. M. Cramer, R. A. Ford, and R. L. Hall, *Food Cosmet. Toxicol.*, 16, 255 (1978).
17. H. R. Roberts, "Food Safety Risk Assessment," paper presented at Peer Review Seminar, Food Safety Council, Palo Alto, California, 1979.
18. N. Mantel and W. R. Bryan, *J. Nat. Cancer Inst.*, 27, 455 (1961).
19. N. Mantel, N. Bohidar, D. Brown, J. Ciminera, and J. Tukey, *Cancer Res.*, 35, 759 (1971).
20. D. Hoel, D. Gaylor, R. Kirschstein, U. Saffiotti, and M. Schneiderman, *J. Toxicol. Environ. Health*, 1, 133 (1975).
21. P. Armitage and R. Doll, "Stochastic Models for Carcinogenesis," *Proceedings of the Fourth Berkeley Symposium on Mathematical Statistics and Probability*, Berkeley, California, 1961.
22. J. Cornfield, *Science*, 198, 693 (1977).
23. J. Cornfield, F. Carlborg, and J. Van Ryzin, "Setting Tolerance on the Basis of Mathematical Treatment of Dose Response Data Extrapolated to Low Doses," *Proceedings of the First International Toxicology Congress*, Lyon, France, 1978.
24. H. Druckrey, "Quantitative Aspects of Chemical Carcinogenesis," in R. T. Truhaut, Ed., *Potential Carcinogenic Hazards from Drugs*, Springer-Verlag, Berlin, 1967, Monograph No. 7.
25. N. Chand and D. G. Hoel, "A Comparison of Models for Determining Safe Levels of Environmental Agents," in F. Proschan and R. J. Serfling, Eds., *Reliability and Biometry, Statistical Analysis of Lifelength*, Society for Industrial and Applied Mathematics, Philadelphia, Pa., 1974, pp. 681–700.
26. K. S. Crump and M. D. Masterman, "Review and Evaluation of Methods of Determining Risks from Chronic Low-Level Carcinogenic Insult," in Office of Technology Assessment, *Environmental Contaminants in Food*, U.S. Government Printing Office, Washington, D.C., 1979, pp. 154–165.
27. R. Peto, "The Carcinogenic Effects of Chronic Exposure to Very Low Levels of Toxic Substances," paper presented at NIEHS Conference on Cancer Risk Estimation, Pinehurst, North Carolina, 1976.
28. K. S. Crump, D. G. Hoel, C. H. Langley, and R. Peto, *Cancer Res.*, 36, 2973 (1976).
29. H. A. Guess, K. S. Crump, and R. Peto, *Cancer Res.*, 37, 3475 (1977).
30. G. S. Watson, *Proc. Nat. Acad. Sci.*, 74, 1341 (1977).
31. Food and Drug Administration, *Fed. Reg.*, 44, 17070 (1979).

32. W. W. Lowrance, *Of Acceptable Risk*, Kaufmann, Los Altos, California, 1976.
33. S. A. Miller, *Food Technol.*, 33 (11), 57 (1979).
34. National Academy of Sciences, *Food Safety Policy: Scientific and Societal Considerations*, Washington, D.C., 1979.
35. I.C. Munro, *Food Technol.*, 33 (11), 43 (1979).
36. R. Zeckhauser, *Food Technol.*, 33 (11), 47 (1979).
37. B. N. LaDu, Jr., *Food Technol.*, 33 (11), 53 (1979).
38. C. J. Brown, *Food Technol.*, 33 (11), 61 (1979).
39. J. M. Turner, *Food Technol.*, 33 (11), 63 (1979).
40. A. S. Clausi, *Food Technol.*, 33 (11), 65 (1979).
41. P. B. Hutt, *Food Drug Cosmet. Law J.*, 33 (10), 558 (1978).
42. Food Safety Council, *Food Technol.*, 34 (3), 79 (1980).

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Founding Trustee

May 23, 1983

The Honorable Orrin G. Hatch
Chairman, Committee on Labor
and Human Resources
United States Senate
SD-G41
Washington, D.C. 20510

Dear Senator Hatch:

I am honored by your invitation of May 12, 1983 to testify before the Committee on Labor and Human Resources of the United States Senate relative to important issues in the area of cancer causation and cancer prevention. I would like to congratulate you and your colleagues in developing a systematic review of the current status of this field as a basis for up-dating regulations and laws bearing on rational sound means of protecting the public.

I do regret, however, that I have a major prior commitment to represent our Institute and, in fact, the United States at a dedication of a major medical research center in Montpelier, France. It would be most difficult to change plans, and I am distressed that I cannot be present in person and review with you and your distinguished colleagues the questions, problems, and opportunities in cancer prevention.

I hope I am permitted to submit the attached document for your use and record. The points I will be making deal with the most impressive advances in our understanding of cancer causation that have been achieved worldwide, but particularly in the United States, in the last ten to twenty years. We have reasonable comprehension of the environmental elements associated with the more important human cancers in the United States that, in turn, can form the basis for feasible and effective preventive maneuvers. In addition, the knowledge we have acquired also shows that certain of the regulatory and legislative approaches need updating. I need not tell you that this knowledge was acquired because of the impressive support through the National Institutes of Health (NIH), National Science Foundation (NSF), and Environmental Protection Agency (EPA) grant and contract support. While in the overall budget of the United States the sums allocated are rel-

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atively small and are normally considered expense items, I would like to suggest that these are not expenses but, indeed, investments that are currently paying off many fold in reduced cancer risk, and thus, diminished expenses in medical care, and above all, are contributing to the health of the American public. We are now at the threshold of even more impressive advances, particularly in the area of nutrition and health. A further investment in this area would essentially solve in the next decade the as yet unknown questions, and I would urge you and your colleagues to consider the past successes as prologue to the definitive solution through the effective reduction of current major premature killing diseases. In my considered opinion, the outstanding questions are fully capable of resolution in our lifetime and will provide future generations of Americans with tools to prevent important kinds of diseases.

Sincerely,

John H. Weisburger, Ph.D., M.D.(h.c.)
Vice President for Research
Director Naylor Dana Institute for
Disease Prevention
Research Professor Pathology New York
Medical College

JHW:CH
enc.

copy: Sen. Edward M. Kennedy, Mass.

REPORT TO THE COMMITTEE ON LABOR AND HUMAN RESOURCES

UNITED STATES SENATE

HEARINGS JUNE 8-10, 1983

New Developments in Research on Cancer Causation and Prevention: Impact on Legislative and Regulatory Activities

This report is provided by John H. Weisburger, Ph.D., M.D. (h.c.) who is Vice President for Research, American Health Foundation, and Director of the Naylor Dana Institute for Disease Prevention in Valhalla, N.Y. 10595-1599. Dr. Weisburger is also Research Professor of Pathology, New York Medical College. From 1949 to 1972, Dr. Weisburger was a member of the staff of the National Cancer Institute, NIH, Bethesda, Md., last as Head, Carcinogen Screening Section, and Director, Bioassay Programs. Dr. Weisburger has been honored by the Federal Government with the National Defense Service Medal and the PHS Meritorious Service Medal, the Japanese Cancer Association Honorary Membership, the Merit Award of the Society of Toxicology, and an M.D. degree (honoris causa) by the University of Umea, Sweden. He is listed in WHO'S WHO, and in the ISI List of 1000 Most Cited Authors. He is an Editor or on the Board of a number of professional journals. Dr. Weisburger has published over 300 research papers and book chapters dealing with the mechanisms of carcinogenesis, with the development of bioassay systems to detect carcinogens, and with the causes and prevention of important forms of human cancers.

A number of legislative and regulatory acts have been instituted in the last thirty years in order to protect the public as regards potential cancer risks. In particular, the food and drug laws were amended in the mid-1950's by the Delaney Clause that requires initiation of action to ban by agencies like the Food and Drug Administration in relation to agents, particularly in the food chain, that might be construed to be carcinogens.

Since the time that the Delaney Clause and other laws and regulations were promulgated, there have been truly impressive advances in a number of scientific and medical research areas bearing on cancer causation.

1. There has been enormous progress in analytical chemistry and instrumental analysis. Thus, very small amounts, and indeed traces of chemicals, can be detected and measured accurately. This advance, in turn, has led to the finding that important elements in the environment used by man, such as certain foods or water, contain specific chemicals that 25 years ago could not be measured. If appropriate tests and bioassays using large dosages show such chemicals to be endowed with "carcinogenic" activity, regulatory agencies have the task of assessing whether or not the presence of very small amounts of such chemicals actually constitute a true carcinogenic risk to man. This has been a most controversial area in the last decade.

It is hoped that new knowledge dealing with the mechanisms of cancer causation and the classification of chemical carcinogens would assist in securing sound background information to provide a rationale for what kind of actions need to be taken, or what kind of situations can be safely accepted, as the case may be.

2. Worldwide research, particularly research in the United States, generously supported in the last 35 years by the American people through grants and contracts from the National Cancer Institute and other Agencies, has led to major key advances in our knowledge of the mechanisms of carcinogenesis. In turn, it is now possible to delineate the complex steps through which a specific chemical can cause cancer, and, furthermore, the intricate interactions that operate at each step. Nonetheless, the broad picture suggests that most chemicals that can cause cancer are converted by appropriate cells and tissues to reactive products that interact in specific ways with the genetic apparatus eventually leading to the development of cancer.

Rapid, efficient and economical tests are available now to ask the question for each environmental chemical whether under conditions prevailing in the environment this particular sequence might operate, and therefore to ask, using such tests, whether a chemical could be carcinogenic. Professor Ames at the University of California, formerly of the NIH, has developed such a test, and Dr. Williams at the Naylor Dana Institute in New York, also formerly of the NIH, has invented another test, complementary in design, function and capability to that of Ames. These and related rapid tests now provide the tools to screen quickly environmental chemicals for possible action on the genetic material, which is now designated as a genotoxic effect.

Most known human carcinogens are genotoxic. Every effort needs to be made to lower the exposure of man to such genotoxic agents to a minimum, although it seems that trace amounts of even powerful genotoxic carcinogens like, for example, the ubiquitous food contaminant Aflatoxin B-1, might normally not present a large disease risk.

However, there are non-genotoxic environmental chemicals that play a role in the subsequent steps of cancer induction through promoting or enhancing mechanisms, a field with new developments that requires detailed research in the future. It is now known, as will be discussed below, that some of the important kinds of cancer seen in the United States appear to be controlled more by such promoting substances, that are not genotoxic, than by the presence of genotoxic agents. Nonetheless, this aspect of the overall carcinogenic process, in which non-genotoxic substances are involved, presents a rather different health risk. Indeed, the promoting effect is highly dependent on the dosage or tissue concentration of the agent, and furthermore, it is reversible, up to a certain point.

A number of widespread contaminants in the environment like chlorinated hydrocarbons in the drinking water have the attributes of non-genotoxic promoters. It is our view that there is no immediate high health risk from the presence of small or trace amounts of such agents. Yet, before mechanistic knowledge was available, certain regulatory actions were attempted at great cost to consumers and communities to remove these contaminants from drinking water. We believe such actions are unnecessary and the focus of activities to reduce human cancer risks should be elsewhere.

Thus, appropriate, rapid and efficient tests can reveal whether a given chemical is genotoxic, or is a promoter or otherwise impinges on the carcinogenic process. Preliminary decisions can then be made quickly and effectively without having to resort to long-term testing of such chemicals in animals, a procedure that is cumbersome, expensive, and by itself not necessarily more relevant. We have developed a "Decision Point Approach" utilizing batteries of carefully selected test systems to ask whether a given environmental chemical might be a health risk. It is hoped that these newer series of tests based on current knowledge of the mechanism of cancer causation can be used effectively by regulatory agencies in pursuing their mandated goals of protecting the public against cancer hazards.

The Delaney Clause fails to take into account the advances described above, and therefore needs revision urgently. It is no longer appropriate to ban a chemical on the sole grounds that it has induced tumors in a given animal test. It is essential to have, as part of the test series, information on its mechanism of action which, in turn, would provide experts in the field a comprehensive set of data to draw the appropriate conclusions on any health risk.

3. At the time that the Delaney Clause and similar regulatory activities were instituted with the desirable aim of eliminating avoidable cancer hazards, there was actually very little firm knowledge about what caused the majority of human cancers. There had been individual case reports demonstrating that specific chemicals had caused cancer in occupational settings, for example, in a chemical factory where large amounts of some chemical intermediates were being manufactured under conditions of poor hygiene and thus high exposure. Therefore the public, lay and scientific alike, was concerned that many forms of human cancer stemmed from chemical exposure. It is clear, therefore, that in light of this feeling, the Congress acted wisely in attempting to regulate and prevent such exposures.

In the last thirty years there have been key discoveries on the causes of important kinds of human cancer. This area is scientifically as exciting and practically as important as the novel developments on the mechanisms of carcinogenesis described above.

These dramatic advances came from the realization that cancer is not a single disease but that there are many different kinds of cancer. Thus, cancer of the lung is distinct from cancer of the colon that is different, in turn, from cancer of the stomach, for example. By careful analysis through diverse techniques and approaches for each human cancer type, it has been clearly established that in different parts of the world, and including in the United States, the majority of human cancers are indeed due to chemicals, but not as normally construed, from contamination of the environment by synthetic chemicals and the activities of industry, but rather are due to specific agents associated with lifestyle.

It is now well established and accepted, but certainly was controversial 30 years ago, that a major human cancer in the United States, cancer of the lung in men and women, is related to smoking, particularly of cigarettes. Also, smokers have a higher risk, through mechanisms that are not yet established, for cancer of the pancreas, kidney and bladder, and in smokers who are also habitual consumers of alcoholic beverages, for head and neck cancers. Current data from the American Cancer Society indicate that 37% of cancers in man and 16% of cancers in women are currently associated with the habit of smoking.

Extensive studies on the mechanism of action of the complex components of cigarette smoke, particularly by Drs. Wynder and Hoffmann and associates of the American Health Foundation, indicate that a relatively small part of the adverse effect of cigarette smoking results from parts of smoke containing genotoxic carcinogens. The major effect stems from the continuing enhancing and promoting action of other components of smoking, a partially reversible action. For these reasons, programs like those of the American Cancer Society to induce smokers to quit have a mechanistically-based rationale for a progressively lower risk which, in fact, has been demonstrated.

More programs are needed to induce individuals, particularly young people, not to start smoking and continue our efforts to get people to stop. This alone would have a major impact in lowering the number of individuals developing cancer, with consequent economic benefits in reduced need for expensive medical care, in having taxpaying people live longer, and, of course, above all, it is ethically proper to avoid preventable diseases, especially those that often have a fatal outcome.

Research, mainly during the last ten years, basically during the life of the enlarged National Cancer Program, has provided exciting leads on the causes of other major human cancer types, those not associated with smoking. These include, in the United States, cancer of the large bowel, breast, prostate, ovary and endometrium, among others, and they account for a large percentage, 52%, of cancers seen. Unlike lung cancer in cigarette smokers, the incidence of which has risen dramatically in the last 50 years, the incidence of these cancers has hardly changed at all. The proper conclusion is that the causes of these cancers have been in the environment for a long time. It is now reasonably sure that these types of cancer are associated with dietary and nutritional customs that also have not changed much.

Indeed, it has been found that the traditional total fat intake in the United States, 40-45% of calories, plays a role in the development of these cancers and, in fact, also in the occurrence of arteriosclerosis and heart disease. The exact mechanisms whereby these effects are exerted are not quite known and are under intensive study. Fat intake translates to cancer risk through non-genotoxic promoting mechanisms, and therefore reduced risk can be secured by lowering fat intake. Similar recommendations have been made for the avoidance of heart disease. In the case of large bowel cancer, there are sound data that the American diet is usually deficient in fiber, and specifically cereal fiber. Any reduction through nutrition would be important with cancers with an incidence of more than 100,000 cases a year.

Current research in this entire field is bound to produce additional parameters in the field of nutrition that can find eventual application to lower risk and prevent important forms of human cancer.

It is hoped the Congress and the Executive Branch will find it possible to expand support for this area, considering where we are now and where we could be in five to ten years. It would seem that this support should not be construed to be an expense item in the Federal budget, but it is a rather remarkably sound, rewarding investment in the future health, and avoidance of major premature killing diseases, of the American public.

In summary, the current legislative and regulatory tools, such as the Delaney Clause at FDA, and similar activities in EPA and other Agencies are focusing large and expensive efforts on the purported aim of cancer prevention. In fact, it is not at all sure that such large efforts are now justified, considering the current status of science. There are, as we discussed, new tools available to detect mutagens and carcinogens efficiently and protect the public at considerably lower costs. It is hoped that the Congress and the Executive Branch will update legislation and actions, and take advantage of the most impressive advances in the varied aspects dealing with cancer causation and cancer prevention. Most human cancers, and in fact heart disease, can be attributed to lifestyle, especially smoking and improper nutrition, too high in total fat and too low in fiber. Research emphasis, and financial support therefore, should be in this area, for successes will translate in effectively lowering the risk of diseases leading to premature death of over 1,100,000 men and women this year. Much progress has been made, because of support by the Federal Government and generous actions by the Congress. The prognosis for the future is even brighter, provided the right direction is followed and supported.

STATEMENT OF
RICHARD A. LILLQUIST
on behalf of the
FLEXIBLE PACKAGING ASSOCIATION
before the
UNITED STATES SENATE COMMITTEE ON LABOR AND HUMAN RESOURCES
concerning the
NEED TO AMEND THE FOOD SAFETY LAWS
June 8, 1983

My name is Richard A. Lillquist, president of the Flexible Packaging Association ("FPA" or "Association"), and I am presenting this statement on behalf of its members. We believe that amendments to the food safety laws must be enacted to remedy some very real regulatory problems facing the flexible packaging industry while continuing to ensure the best protection of the public food supply.

Before commenting on the bill, it may be helpful to briefly describe the Flexible Packaging Association and the industry it represents. FPA is a trade association representing over 170 firms which manufacture flexible packaging or supply materials or machinery for use in the manufacture of flexible packaging. The term flexible packaging encompasses pliable or non-rigid containers and wraps converted into packaging products. Both the food and health care markets rely on flexible packaging. Some examples of the hundreds of different flexible packaging products are bread bags, meat packaging, and pouches for mixes, snack foods and frozen foods. Paper, plastic films and aluminum are the basic materials that form the industry's products. These are coated, combined and converted with sophisticated technology to create packaging systems for use in our homes, schools, restaurants and in a variety of environments ranging from parks to battlefields, from hospitals to spacecraft.

There are more than 900 flexible packaging plants in the United States which are responsible for producing over 100 billion packages a year. The Association represents nearly 80% of the flexible packaging sold in the United States.

A. Existing Statutory System

The existing statutory system is based on the Food Additives Amendment of 1958. That legislation added a new definition to the Federal Food, Drug, and Cosmetic Act ("Act") for a "food additive," which was defined as "any substance the intended use of which is expected to reasonably result, directly or indirectly for use in . . . packaging, transporting, or holding food . . . ." Substances that are generally recognized as safe (GRAS) by qualified experts or that the Food and Drug Administration (FDA) had sanctioned before 1958 are not included in the definition.

This statutory language presents the question of whether packaging material may "reasonably be expected" to become a component of food, that is, whether a component of the packaging migrates into the food. Obviously, the producer or packager of food and health care products does not normally intend to have the packaging migrate into the contained product. The purpose of the packaging is to maintain the integrity of the contents for as long as possible.

Unfortunately, the present law does not distinguish between substances that are directly and intentionally added to food in sufficient quantity to achieve a technical effect and trace migration from packaging materials. The unnecessary burdens that the flexible packaging industry faces under the current system result from subjecting packaging to the same statutory plan as intentional food additives. Our recognition of the urgent need for separate treatment is based on the different regulatory questions to be answered, the dramatic advances in analytical techniques used to test for migration, and the manner in which FDA has handled packaging questions over the last twenty years.

Under existing section 409 of the Act, any food additive, including those contained in food-packaging materials, is deemed unsafe unless it is used in conformity with an investigational use exemption or a regulation issued by FDA. To obtain such a regulation, the manufacturer must file a petition with FDA. Based on this submission, the Agency determines the safety of the packaging material under intended conditions of use. This includes an evaluation under the prohibitions of the Delaney Clause. In addition, the rulemaking encompasses consideration of the probable consumption of the additive, the cummulative effect of the additive in the diet and other safety factors.

According to the statutory language, the regulation establishing the approved use or an order denying the petition must be issued within 90 days after the date of filing the petition. FDA may extend the deadline an additional 90 days if more time is needed to reach a conclusion. Although the statutory timetable is explicit, it generally takes two, three or more years to obtain a regulation from FDA. In our opinion, this delay is largely attributable to a statutory plan that not only applies the same procedural system to both direct and indirect additives but also requires FDA to engage in a rulemaking proceeding in every case.

B. Packaging Presents Different Health and Regulatory Concerns

Prior to marketing, certain questions must be answered when a new packaging substance, a new combination of substances or a new application for existing packaging material is developed. The manufacturer will attempt to establish whether the particular food-packaging application is subject to an existing FDA regulation. If not, the packaging may be generally recognized as safe or prior-sanctioned. Another inquiry, based on the statutory language, is whether any substance contained in the packaging material may reasonably be expected to migrate into the food.

With most food packaging, the primary inquiry is whether any component of the packaging migrates into food, and if so, how much migrates. Often, once information on extraction studies is obtained, toxicological information plays a minor role because of the insignificant amount of extractions. In this sense, the questions facing FDA are distinct from those involved with direct food additives where the amount of the substance in the food is well-established.

To state the difference quantitatively, direct food additives are seldom less than fractional percentages of the food, for example 0.01%. In contrast, migration of food packaging into food is described in terms of parts per million (ppm) or billion (ppb). The difference may be easier to conceptualize when the concentration is explained in terms of time. For example, 0.01% of a year is 52.5

minutes; 1 ppm of a year is 0.525 minutes; and 1 ppb of a year is 0.000525 minutes. Thus, even though the health concerns are different and a packaging substance migrates to food in insignificant amounts, the manufacturer must still go through a food additive petition process which may take three or more years.

C. Changes in Analytical Techniques

The process of determining whether a substance may be reasonably expected to migrate into food has been profoundly affected by advances in the analytical techniques that scientists use to determine whether migration has occurred. When the Food Additives Amendment was passed in 1958, analytical chemists generally ran extraction studies with a sensitivity of method in the low ppm. Thus, if the extraction study showed migration, the substance could reasonably be expected to be present in food in the range of a part per million or more. Today, many substances can be detected in parts per trillion, and commonly-run detection studies measure in parts per billion. In the foreseeable future, scientists may be able to detect a single molecule or atom within a mixture.

Because of these scientific developments, many packaging substances not anticipated by Congress to be subject to regulation have been swept within the statutory phrase "reasonably expected" to become a component of food. This inclusion is unreasonable; migration at very low levels presents no meaningful risk, and the expenditure of regulatory and private resources is unwarranted.

D. FDA Regulation

Additional difficulty has been generated by FDA's interpretation and administration of the Act. In essence, FDA has adopted a position under which essentially everything that comes in contact with food is subject to the food additive petition process unless it qualifies for some statutory exemption. This history is detailed in testimony submitted by The Society of the Plastics Industry, Inc. (SPI). I will not duplicate that testimony here but simply draw the Committee's attention to it for substantiation of the general statements made here. Rather than pursuing a general chronology of FDA regulation from 1958 to the present, I would like to present one example of the difficulties which a new packaging material faces under the current system.

E. The Retortable Pouch

The retortable pouch is basically a flexible can. A typical pouch consists of three laminated layers. The exterior layer consists of a substance such as polyester, chosen for its toughness, durability and printing compatibility. The center layer is an aluminum foil which acts as a moisture, oxygen and light barrier. The inside layer, which contacts the food is a plastic film such as polypropylene. It is suitable for food-contact applications and provides an excellent heat seal.

The advantages of the retortable pouch over the conventional can are impressive. Energy and quality are key factors. Producing an eight-ounce pouch and an outer paperboard box requires 1,934 British Thermal Units (BTUs). This compares to 3,560 BTUs for an equivalent-sized can and label or 3,174 BTUs for a glass jar. Because of the thin profile of the pouch as compared to the can, food in the pouch heats more rapidly and uniformly, thus reducing processing time. The reduced processing also yields a product with better flavor and texture than that achievable from typical can processing. Improved texture and flavor also mean that foods packaged in a retortable pouch are qualitatively competitive with frozen foods. Obviously, since the product in the retortable pouch is stored on the shelf without refrigeration, there would be additional energy savings from this factor when compared to frozen food.

The reduced weight of the pouch increases transportation efficiency. One thousand empty eight-ounce pouches weigh approximately 12 pounds while one thousand empty eight-ounce cans weigh about 109 pounds. Incidentally, a Defense Department spokesman indicated that the retortable pouch would also reduce dependence on imported tin.[1/] Thus, the retortable pouch even carries strategic mineral considerations.

Our story of the retortable pouch begins in 1958, the same year that the Food Additives Amendment was enacted. In that year, the U.S. Army laboratory at Natick, Massachusetts began extensive testing of flexible pouches. Later, commerical food processors and packagers worked with the laboratory. However, public marketing first occurred overseas. By the early 1970s, the retortable pouch was marketed in Japan, Italy, Sweden, Denmark, and England.

[1/] Lieutenant Colonel Avalon L. Dungan, Army Quartermaster Corps, made this statement in a speech before the National Food Processors Association (NFPA). See, Food Chemical News p. 15 (Feb. 25, 1980).

One of the first proposed applications for domestic use of the retortable pouch was the packaging of meat and poultry products. This involved the U.S. Department of Agriculture (USDA), which authorized test production in October, 1974. But, in March, 1975, USDA sent letters to the manufacturers asking for more data.

In April, 1975, FDA began questioning manufacturers of retortable pouches. FDA was concerned that a by-product of a residue in the adhesive used to bond the layers might penetrate the layer surrounding the food and migrate into the food.[2/] The following month, USDA rescinded its approval pending FDA determination of food additive status.

In response to this changed status for retortable pouches, FDA held a meeting on June 6, 1975, that was attended by over 150 industry representatives. We bring this meeting to your attention because it highlights a problem that results from the present system. As you are aware, the current statutory plan requires that FDA promulgate a regulation in response to an appropriate food additive petition. There are obvious difficulties in promulgating any regulation, and the retortable pouch shows a difficulty that FDA faces under that system.

The meeting was headed by Richard Ronk, then Director of FDA's Food and Color Additives Division, and now Deputy Director of the Bureau of Foods.

2/ FDA was concerned with isocyanate fractions. A new National Cancer Institute (NCI) study suggested that 2,4-diaminotoluene, also known as toluene diamine (TDA) was a moderate carcinogen. An adhesive component, toluene diisocyanate (TDI) could become TDA at levels of 3 ppb if TDI migrated through the inner layer and was exposed to water in the food.

At the meeting, Mr. Ronk stated that existing regulations appeared to cover the use of the pouch components that FDA questioned but that this apparent approval was not intended by FDA. It was a problem inherent in the rulemaking process.[3] In addition, Mr. Ronk indicated that a new rulemaking proceeding was likely to be delayed by other demands on Agency resources.

Advances in analytical techniques compounded the problem. Existing FDA regulations for the adhesive required a functional barrier between the food and the adhesive, although the term "functional barrier" has never been defined. Since all films and coatings are permeable to some degree, improved analytical techniques created the possibility of finding some adhesive migration. If this occurred, then the film would not be considered a "functional barrier" and the use not in compliance with the regulation. Moreover, even the detection of a single molecule of the original adhesive that might have migrated through the film might trigger unrealistically harsh results under the Delaney Clause.

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[3] Mr. Ronk stated (Hearing transcript at 4-5):

> I think everyone that is initiated, has been initiated into this business, has as I have been over the last few years, realizes that there is no way that you can write a regulation that can anticipate every possible situation that something is going to be put and if you look at the polyolefins in terms of retortable conditions . . . they haven't been evaluated in those terms.

The meeting thus highlighted another difficulty with FDA enforcement. FDA has never established a level of insignificant migration.[4/] Today, FDA has yet to determine what level in particular or as a general matter it would deem as insignificant. This position plainly conflicts with the controlling law on the subject.[5/]

Subsequent to the meeting and at FDA's suggestion, several manufacturers filed food additive petitions for the adhesive used in the pouches. Extraction studies conducted under exaggerated time and temperature conditions showed migration of about 3 ppb of TDI, an adhesive component. FDA reviewed these extraction studies and estimated the potential risk if the TDI became TDA in the presence of water in the food. The Agency's technical staff concluded that any risk presented by this migration was plainly insignificant.

Industry members involved in the process report that the FDA technical staff involved with the project were cooperative and cordial. At the conclusion of the scientific safety review, the FDA technical staff and their industry counterparts were drafting proposed regulations to permit use of the adhesive in the retortable pouch.

The resolution of scientific and safety question did not, however, produce a happy ending. According to informal reports, when FDA's technical staff report reached the General Counsel's office, it was firmly rejected. The lawyers found that since a by-product of a trace residue in the adhesive might

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[4/] Hearing transcript at 30.

[5/] Monsanto Co. v. Kennedy, 613 F.2d 947 (D.C. Cir. 1979).

migrate, and since it had been implicated in the NCI study, use of the substance was banned under the Delaney Clause. Parenthetically, I should note here that the adhesive in question was and continues to be used extensively in Europe, Canada and Japan without any indication of any health problem.

At this point, after years of development and testing, industry had to start the process all over again. Given this regulatory experience, the research focused on substitute substances subject to an existing regulation that would obviate the need for a rulemaking. Ultimately, technology was developed to use a bonding agent which complied with the can coating regulations.

This effort to gear research and development to fit within existing regulations had its price. The substitute adhesive was more expensive and more difficult to produce. Thus, productivity was lowered and only a few manufacturers had the equipment to produce it. Ironically, there was much less product history of food being stored in pouches made with the substitute than with the originally-specified adhesive.

The retortable pouches produced in the United States today are made with this substitute bonding agent. The food additive petitions for the aromatic polyurethane adhesive were never approved. Indeed, in 1981, FDA contacted the firms that filed the petitions and indicated that the Agency was trying to clear up a backlog of petitions and would be rejecting these on the basis of carcinogen migration unless the petitions were withdrawn. Fearing that rejection of the petitions might be incorrectly associated with existing pouches and create disasterous publicity, the petitions were withdrawn in early 1982.6/ New

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6/ 47 Fed. Reg. 1334 (Jan. 12, 1982).

petitions for aliphatic polyurethane adhesives were filed later in 1982. Just this year, in January and April, 1983, FDA approved these petitions, about eight years after a "non-problem" was initially noted.[7/]

In sum, this entire episode demonstrates how the present law defeats the efforts of good people in government and industry who are trying to provide safe, economical, and improved products for the public. It is a sad triumph of outdated law over reason.

F. Conclusion

Being responsible members of the business community, we recognize the need for protecting the public safety. We are proud that packaging has not presented a health risk to the consumer. Unfortunately, the regulatory system currently imposes a number of unnecessary hurdles which discourage innovation in packaging and demonstrate the need to revise the underlying law. The Flexible Packaging Association believes that a number of improvements should be adopted.

Congress should bring the substantive provisions of our food safety laws into line with modern scientific advances and provide meaningful guidance to FDA in making safety determinations. For example, the term "safe" needs to be defined. One formulation might require a showing that any risks under the intended conditions of use are negligible. Such a change would maintain the safety provisions of the current law while rejecting the unattainable concept of absolute safety or zero risk.

Changes in the clearance process for food packaging are also needed to reduce the unnecessary regulatory delay and expense imposed by the existing system while encouraging safe and efficient innovation in packaging. Ultimately, it is the consumer that will benefit from these advances. A good starting point for these legislative changes is the draft language prepared by the Sub-Cabinet Council Working Group on Food Safety Reform.

On behalf of FPA, I would like to express our appreciation for this opportunity to comment on the need for reform.

[7/] Food Chemical News, pp. 23-24 (Jan. 10, 1983); p. 60 (Apr. 11, 1983); p. 60 (Apr. 25, 1983).

STATEMENT OF
THE AMERICAN FEED MANUFACTURERS ASSOCIATION
TO THE
COMMITTEE ON LABOR & HUMAN RESOURCES
UNITED STATES SENATE
ON THE NEED FOR MODERNIZATION OF THE NATION'S FOOD SAFETY LAWS

JUNE, 1983

Mr. Chairman and Members of the Committee:

The American Feed Manufacturers Association (AFMA) appreciates the opportunity to contribute to the official hearing record of the U.S. Senate Committee on Labor & Human Resources regarding the need for reform and modernization of the nation's food safety laws.

For 75 years AFMA has been the national trade association representing the manufacturers of more than 70% of the primary formula livestock and poultry feed sold in the U.S. As such, AFMA's nearly 700 member companies are vitally concerned that contemporary science be brought to bear on existing food safety laws, and that a system of interpretation and enforcement be used that is equitable and which provides adequate protection for human health.

It was over a quarter century ago, in 1958, when the last major food safety amendments were passed by Congress. The administration of these laws by the Food & Drug Administration and the U.S. Department of Agriculture has resulted in a food supply unrivaled for its safety, wholesomeness, variety and availability. However, regulatory incidents in recent years--most notably nitrites and saccharin--coupled with scientific and technological achievements in the intervening decades, have, as Chairman Hatch stated in his opening remarks, "brought new complexities and intracies to the implementation of our food safety laws."

AREAS IN NEED OF REVIEW/CHANGE

AFMA recognizes the broad consensus among industry groups, the Administration and some individuals to support general areas of review and prospective modernization. Those areas which AFMA has identified as being in need of modification include:

1.THE DELANEY CLAUSE: Sec. 409(c)(6)(A) of the Food, Drug & Cosmetic Act includes the so-called Delaney anti-cancer clauses, which essentially call for a zero-risk determination in the review of suspected carcinogenic substances in the food supply. It is this clause which has caused debate over the inflexibility of its application, especially given the current scientific ability to detect the presence of a suspected or known carcinogen in amounts as minute as parts per trillion.

AFMA has pointed to inadequacies which exist in applying current science under the Delaney language. These include the appropriateness whether data obtained from animal testing is relevant to man, the lack of exposure level criteria in determining risk to humans, or the lack of risk assessment procedures in evaluating the significance of animal drug residues in edible tissues.

AFMA supports the concept of risk assessment. Science is increasingly able to identify extremely small quantities of substances in edible tissues. It is appropriate that science also be used to evaluate the degree of suspected risk presented.

AFMA believes that legislative change should include modification of the Delaney Clause to specifically provide for scientific review and consideration of whether a subtance that causes cancer in animals actually presents a risk to humans under the intended conditions of its use. We believe that such a modification would allow the government to take advantage the best available contemporary science when considering the safety of a substance, while at the same time adquately protecting human health.

2. DEFINITION OF SAFE: Directly related to the perceived inflexibility of the Delaney Clause, is the current interpretation of "safe," as defined in the legislative history of the 1958 amendments to the FDCA. Broadly construed to mean "reasonable certainty of no harm under intended conditions of use," this interpretation has generally been used as a "no risk" standard. Given the abilities of current science, this interpretation is unacceptable. The association believes a workable definition of safe is necessary. The standard set by the Congress for determining whether a substance in the food supply is safe should include requiring FDA and other agencies to assess all available information on the extent to which the substance may pose a threat to human health. Such a definition, incorporated into the act, would also go far to minimize the inevitable blurring of congressional intent caused by changes in administration.

3. FOOD ADDITIVES AND TRADITIONAL FOODS: It has been suggested by some that portions of the current Sec. 201(s) of the FDCA, which deals with substances generally recogonized as safe (GRAS), be eliminated. AFMA opposes such a change, since this would mean, practically speaking, that a substance no matter how basic, such as soybean meal, could not be approved by FDA for use except through the agency's food additive clearance procedures. For example, if a feed

mixer chose to use a common substance such as flaxseed meal as part of the ration for a specie such as duck or goats, where it had not previously been fed, the substance would have to be cleared under Sec. 409 food additive clearance procedures since any prior history of safe use would no longer bear on the decision. This would eliminate any ability by FDA to use common sense about common substances.

4. MEDICATED FEEDS: AFMA's consistent philosophical position on statutory revision to those portions of the FDCA which apply to medicated animal feeds is that if a substance poses a significant risk to human health, it should be regulated and all users of that substance--whether commercial manufacturers or livestock producers--be regulated equally. If a substance does not pose such a risk to human health, then that substance should be subject to no more than minimum regulation, or where a substance is proven to be safe, no regulation.

Currently, some establishments using less potent subtances are subject to FDA pre-clearance procedures and should be deregulated.

AFMA's recommendations for change in this area are designed to establish consistent, rational regulation of all persons performing the same function with the same product. At the same time, AFMA recommends substantial deregulation of persons using relatively dilute drug sources.

AFMA again thanks the Committee for the opportunity to participate in this vital process.

STATEMENT OF THE
FLAVOR AND EXTRACT MANUFACTURERS
FOR THE RECORD OF THE COMMITTEE
ON
UNITED STATES SENATE
LABOR AND HUMAN RESOURCES,
HEARINGS ON FOOD SAFETY

June 24, 1983

The Flavor and Extract Manufacturers' Association of the U.S. (FEMA) appreciates the opportunity to comment on the record of the Senate Committee on Labor and Human Resources on the issue of recision of the Federal Food, Drug and Cosmetic Act. FEMA represents the overwhelming majority of flavor manufacturers in the U.S. who manufacture most of the food flavors sold in the U.S. The safety of our food supply is of paramount importance to the members of FEMA and therefore we commend the Committee for undertaking this review of the adequacy of our food safety laws in the light of contemporary science.

The record of this hearing demonstrates beyond dispute that scientific advances have justified the Committee's review of the Federal Food, Drug and Cosmetic Act. Representatives of the scientific community, consumer groups and industry have presented their views on such issues as the meaning of "safe", the Delaney Clause, risk assessment, benefits consideration, and peer review.

However, there is one provision of the statute which has kept pace with science over the years since its enactment and which serves as a model of responsible industry self-regulation under the supervision of the FDA. This provision, which governs substances which are "generally recognized as safe" (GRAS), does not require legislative amendments because it has worked well. It is one of those provisions of a basically sound statute which should not be amended.

Section 201(s) of the Federal Food, Drug and Cosmetic Act provides an exclusion from the statutory definition of food additive for substances "generally recognized as safe" (GRAS) under conditions of use by qualified experts. For over twenty years, FEMA has been guided by a panel of independent experts highly qualified by scientific training and long experience to evaluate the safety of flavor materials. On the basis of opinions of these experts, FEMA published lists (enclosed) of materials which are considered by the Panel to be GRAS under the conditions of intended use within the meaning of the law. These lists, which have been provided to the Food and Drug Administration prior to publication, [1] have provided benefits to the public, the FDA and the industry as described more fully below.

Many years ago, upon the recommendation of FDA, FEMA adopted the policy of publication in the scientific literature as essential to "general recognition". This provides further assurance of the reliability of the scientific data relied upon in safety evaluation. This is because peer review usually occurs prior to publication and readers are free to respond in the literature if they disagree with a finding. In short, the FEMA Expert Panel's determinations of GRAS status are published in the open literature where they must withstand the scrutiny of the scientific community.

"General recognition" by qualified experts automatically incorporates scientific advances into the statutory standard governing the use of these ingredients. Qualified experts keep abreast of advances in their field and in tune with the mainstream of scientific thinking. Therefore, this provision of the statute assures safety decisions based on contemporary science.

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[1] Many substances were reviewed by the Expert Panel at the suggestion of FDA. In addition, FDA's regulations for natural and synthetic flavor substances (21 C.F.R. §§ 172.510, 172,515) are largely based upon evaluations by the Panel. See, Oser and Hall, "Criteria Employed by the Expert Panel of FEMA For the GRAS Evaluation of Flavoring Substances," 15 FD. COSMET. TOXICOL. 457-466 (1977) (Enclosed).

Yet another advantage of the GRAS concept is that it frees the FDA from having to devote its scarce resources to the regulation of substances that present little, if any, public health concerns. Many GRAS substances have been used in human foods since time immemorial. This long history of safe use in humans provides some assurance of their relative insignificance to the public health. Still other GRAS substances, flavors in particular, are used in such miniscule quantities that intense FDA scrutiny of their use is unnecessary. Nevertheless, FDA is always free to challenge the GRAS status of a substance when evidence shows that it may in fact be significant to the public health. In short, the GRAS concept reflects a sound Congressional determination that FDA's resources are best expended evaluating substances that are significant to the public health.

In conclusion, the record of this hearing shows that there are provisions of the food safety law that merit Congressional consideration of the need for amendments due to the advances of science. In contrast, the GRAS concept has helped assure safety decisions based on contemporary science, obviated the expenditure of scarce FDA resources on substances of little, if any, public health significance and allowed industry to innovate. The GRAS provision has been effective and Congressional consideration of amendments to the food safety provisions of the Federal Food, Drug and Cosmetic Act should be directed to those provisions more needful of modernization.

(Note: In the interest of economy, the appendix material accompanying this statement was retained in the files of the Committe where it may be researched upon request.)

June 9, 1983

STATEMENT BY
FRANK MANNO, CHAIRMAN
of the
LABELING AND GMPs COMMITTEE
of the
INDEPENDENT BAKERS ASSOCIATION
before the
UNITED STATES SENATE
COMMITTEE ON LABOR AND HUMAN RESOURCES
FOOD SAFETY

Mr. Chairman, my name is Frank Manno. I am President of Schafer's Bakeries, Inc. of Lansing, Michigan. I serve as the Chairman of the Labeling and Good Manufacturing Practices (GMPs) Committee of the Independent Bakers Association (IBA) and appear today in that capacity. IBA is a national trade asciation comprised of over 300 independent small and medium sized wholesale bakeries, most of which are family owned. Collectively, we produce nearly half of the wholesale bread sold thoughout the United States.

Over the past few years, sentiment within the scientific community to relax and re-address current Food Safety law based on the principle of zero-risk has grown. Under the Delaney Clause, all additives found or thought to contain minor amounts of carcinogenic chemicals must be banned by the Food and Drug Administration (FDA).

This strict Food Safety policy has created numerous problems for the food industry due to the rapid advancement of technology which allows scientists to analyze foods to the parts per billion. As a result, many necessary and important additives, both natural and man-made, which are found to contain trace amounts of carcinogenic chemicals face the probability of being banned by the FDA unless Congress takes action to restrain the agency as in the case of the popular sweetener saccharin.

Presently, Food Safety law fails to weigh the costs of banning a chemical versus the public health benefits to determine the net effect of such a prohibition. As more basic and widely used additives are found to cause cancer prompting Congressional action to allow their continued use, the credibility of the Delaney Clause will erode. Therefore, given the technological capabilities of the scientific community in analyzing foods and the potential havoc that could be created if an essential ingredient was found to have the slightest risk of causing cancer, IBA supports Congressional revision of existing Food Safety Law.

IBA would like to point out that if the Congress establishes a new concept of "acceptable risk", independent bakers and other food producers would be using ingredients they know might cause cancer and thus would be vulnerable to civil damage suits. Although the food industry could protect itself by displaying warning labels on food packages similar to those used on cigarettes, i.e. Eating This Food Product May Be Hazardous to Your Health, consumer acceptance of this protection method is unlikely. Therefore other steps must be taken to protect the food industry from civil damage suits if the FDA approved ingredients which present slight risks actually turn out to cause serious health problems. IBA believes that Congress should include a clause relieving food producers of the responsibility for the consequences of decisions made by the FDA in new Food Safety legislation.

Failure to free independent bakers and other food producers from liability of scientific determinations far beyond their skill and knowledge could open the doors to financial destruction of the food industry through endless law suits. Congress must not overlook this potential consequence of implementing acceptable risk as it attempts to reform present Food Safety law. The widespread and serious implications of a loophole of this nature and magnitude are obvious and Congress must act now to prevent such an unfortunate oversight!

In closing, I would like to reiterate IBA's support of Food Safety law reform permitting the consideration of costs versus benefits in FDA decision making and stress the importance of relieving independent bakers and other food producers from liability for using ingredients approved by the FDA but known to pose a minute risk of causing cancer. I respectfully urge you to keep in mind the grave impact civil damage suits could have on the entire U.S. food industry as you rewrite current Food Safety Law.

Mr. Chairman, I thank you for the opportunity to submit this statement regarding Food Safety law reform.

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AMERICAN PAPER INSTITUTE
NATIONAL FOREST PRODUCTS ASSOCIATION

API/NFPA Environmental and Health Program
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Michael C. Farrar
Vice President
202-797-5764

June 20, 1983

The Honorable Orrin G. Hatch, Chairman
Committee on Labor and Human Resources
United States Senate
Room 428, Dirksen Office Building
Washington, D. C. 20510

The Honorable Edward M. Kennedy
Ranking Minority Member
Senate Labor and Human Resources Committee
428 Dirksen Office Building
Washington, D. C. 20510

Re: Food Safety Legislation

Dear Senators:

The American Paper Institute (API) submits the following testimony on food safety legislation, and respectfully requests that it be entered into the record of your Committee's hearings on food safety legislation held June 8, 9 and 10, 1983.

API is the national trade association for 175 firms that produce pulp, paper and paperboard throughout the country. Many of these firms manufacture food packaging material, sales of which amount to billions of dollars annually in this country. Because of the possibility that minute quantities of substances contained in paper and paperboard may migrate to food, many food packaging materials are subject to the food safety provisions of the Federal Food, Drug and Cosmetic Act (Act). Such materials are likely to be affected by various proposals to amend the Act's provisions regarding food additives. This letter sets forth API's general views on food safety legislation.

API believes that food packaging constituents should be subject to appropriate regulatory review to the extent they may meaningfully affect the safety of food. Accordingly, it strongly endorses the basic intent of such proposals as last term's S. 1442 and the draft bill of the Sub-Cabinet Council Working Group to establish a flexible and realistic regulatory policy placing increased reliance on significant risk assessment procedures.

Under current law, food packaging materials are evaluated under an absolute safety standard, the same standard required for direct food additives. Application of that standard causes overly rigid regulatory responses to any adverse indications about constituents of food packaging materials. Because of the cost and delay caused by regulatory approvals, it also inhibits innovation in the development and marketing of new food packaging materials. Because the amount of any packaging component that may migrate to food is exceedingly small, such components should not be subject to the same rigorous and lengthy review procedures required for direct food additives. Accordingly, API believes FDA should be encouraged to employ risk assessment procedures to be used in determining the safety of indirect food additives. In particular, API supports an approach that would: (1) exclude from the concept of food additive any packaging substance that becomes part of food in only *de minimis* amounts; (2) provide for expedited review of classes of food contact substances that clearly pose no significant risk to health (*e.g.*, dry food packaging); (3) tailor the amount of testing required to the potential health risk; and (4) not mandate immediate elimination of indirect food additives in extensive use where any potential health problems do not pose imminent danger.

1. *De minimis Approach for Food Contact Substances*.

API believes that any packaging substance that becomes part of food in only *de minimis* amounts should be allowed to be marketed without a food additive regulation. Such an approach would be consistent with the intent of the Food Additives Amendment of 1958 to exclude a substance from the statutory definition of food additive unless FDA determines "with a fair degree of confidence that a substance migrates into food in more than insignificant amounts." *Monsanto Co. v. Kennedy*, 613 F.2d 947,955 (D.C. Cir. 1979).[1]

API would not support, however, any legislation that would condition marketing of food contact substances on issuance of an FDA advisory opinion confirming that migration is _de minimis_. Requiring regulatory confirmation would reintroduce the premarket approval process, a result clearly not envisioned by the current proposals to amend the food safety provisions of the Act, and would burden the marketing of such substances with the regulatory delays that characterize the current food additive approval process. This is precisely what the _de minimis_ approach is intended to avoid.

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[1] The court in *Monsanto* did not specify when and under what circumstances migration of a substance into food is to be considered *de minimis*. But the court made it clear that there should be "latitude inherent in the statutory scheme to avoid literal application of 'food additive' in those *de minimis* situations that . . .clearly present no public health or safety concerns." 613F.2d at 954. API agrees with this sound priniciple.

2. _Expedited Review for Certain Food Contact Substances_.

API also supports expedited review of classes of food contact substances that clearly pose no significant risk to human health. Such a procedure was embodied in the draft bill of the Sub-Cabinet Working Group on Food Safety as well as in the Staff Working Draft of the Committee on Labor and Human Resources. Because indirect food additives, including many paper food packaging components, must under current law be reviewed for safety through the same rigorous procedures required for direct food additives, approval of a new paper food packaging additive may require as long as two years. Such delays adversely affect product innovation and significantly increase the cost of packaging. Expedited review, such as that provided by a regulatory approval deadline, would avert plainly unnecessary delay in approval of petitions for food contact substances that migrate to food but which pose no significant risk to human health.

3. Testing Requirements Governing Food Contact Substances.

API endorses the principle that testing requirements should be tailored to the potential health risk posed by food additives. This approach will provide for efficient testing and review of substances unlikely to pose serious risk, and at the same time will allow greater resources to be devoted to testing and evaluating substances that are more likely to be harmful.

Any amendments to the Act, however, should not provide for establishment of tailored testing requirements through regulations. Scientific knowledge relating to toxicological and migration testing methods and interpretation of data is ever-changing and dynamic. To establish such testing methods and analysis of data by inflexible and static rules, which can be amended only through the time-consuming procedures prescribed by the Administrative Procedure Act, would bind FDA and industry to practices that will quickly become outdated. Accordingly, any legislation should allow FDA to establish through flexible guidelines the quality and quantity of testing required to support a food additive petition. Such guidelines should be developed with opportunity for public input, and should reflect testing methods that are generally agreed upon by the scientific community.

4. Gradual Phase-out of Indirect Food Additives Found to be Unsafe.

The Act does not now authorize gradual elimination of additives determined to be unsafe. Thus, any additive found to be unsafe must immediately be removed from the market, regardless of expense, even where a more deliberate process would reduce unnecessary expense and disruption to industry and the public without posing significant risks to public health. Legislation that would explicitly authorize a gradual elimination process is thus appropriate, especially for food contact substances, for which exposure levels are usually minute. Where questions of safety warranting further study have been raised about a substance, this phase-out process should not be undertaken until such study has been completed and FDA has evaluated the results and judged that removal is required.

API hopes these comments will be helpful in the Committee's efforts to enact appropriate food safety legislation. As the representative of a large, significantly affected industry, API would also welcome the opportunity to comment on specific proposals developed by the Committee and its staff and to testify in hearings before the Committee.

Sincerely,
Michael C. Farrar
Michael C. Farrar

MCF/JLF/lr

Copies sent to the following people:

Senator Dan Quayle, Utah
Senator Don Nickles, Oklahoma
Senator Jeremiah Denton, Alabama
Senator Lowell P. Weicker, Jr., Connecticut
Senator Charles E. Grassley, Iowa
Senator Paula Hawkins, Florida
Senator Gordon J. Humphrey, New Hampshire
Senator John East, North Carolina
Senator Jennings Randolph, West Virginia
Senator Claiborne Pell, Rhode Island
Senator Thomas F. Eagleton, Missouri
Senator Donald W. Reigle, Jr., Michigan
Senator Howard M. Metzenbaum, Ohio
Senator Spark M. Matsunaga, Hawaii
Senator Christopher Dodd, Connecticut

The Honorable Margaret M. Heckler
Secretary, Department of Health and Human Services

The Honorable John R. Block
Secretary, Department of Agriculture

The Honorable Arthur Hull Hayes
Commissioner, Food and Drug Administration

The Honorable C. W. McMillan
Assistant Secretary for Marketing and Inspection Services
Department of Agriculture

Mr. Steve Grossman
Mr. Westley H. Clark
Dr. David Kessler

NATIONAL
FARMERS
UNION

June 7, 1983

The Honorable Orrin Hatch
Chairman
Labor and Human Resources Committee
United States Senate
Washington, D. C. 20510

Dear Senator Hatch:

In your consideration and development of a hearing record on the Nation's Food Safety Laws and Regulations, June 8, 9, and 10, we respectfully request that you include this letter as a part of the hearing record.

Delegates to the National Farmers Union convention, meeting in San Diego, California, February 27 - March 2, 1983, adopted the following policy on dietary guidance:

> "We urge that the Delaney Amendment be amended to reflect advances in technology and not unduly inhibit the production and processing of food products.
>
> "We believe that comprehensive and unbiased research should precede any official dietary advice regarding the relationship between diet and health."

America's farmers have used scientific and technological advancements to greatly increase their productivity and so assure an abundant, stable and nutritious supply of food for the citizens of this nation. They have an overriding personal and professional involvement in the issues which you will review.

Thank you for your attention in this matter.

Sincerely,

Ruth E Kobell

Ruth E. Kobell
Legislative Assistant

REK:kls

cc: Members of the Labor and Human Resources Committee

united fresh fruit and vegetable association
NORTH WASHINGTON AT MADISON, ALEXANDRIA, VIRGINIA 22314, 703/836-3410, Cable: UNIFRESH

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the fresh approach

July 1, 1983

The Honorable Orrin G. Hatch
U. S. Senate
Washington, D.C. 20510

Dear Chairman Hatch:

United and its 2500 member companies support modernization of our nation's food safety laws. The enclosed statement, which has been submitted for the record to the Committee on Labor and Human Resources, details the position of the association.

United commends you and the committee for addressing this important and timely subject and looks forward to cooperating with you and your staff to develop reasonable legislation.

Sincerely,

J Patrick Boyle

J. Patrick Boyle
Government Affairs Counsel

JPB:m
Enclosure

BEFORE THE

COMMITTEE ON LABOR AND HUMAN RESOURCES

U.S. SENATE

COMMENTS

OF THE

UNITED FRESH FRUIT AND VEGETABLE ASSOCIATION

ON

REFORM OF FOOD SAFETY LAW

June 30, 1983

Submitted by: Roger J. Stroh
Vice President
Public Affairs

J. Patrick Boyle
Gvt. Affairs Counsel

The United Fresh Fruit and Vegetable Association (United) headquartered in Alexandria, Virginia, wishes to commend Chairman Hatch and the Committee on Labor and Human Resources for conducting three days of informative and valuable hearings on the need to reform our nation's food safety laws and appreciates this opportunity to comment upon this important issue.

Briefly, United is the national trade association for the fresh fruit and vegetable industry. Its 2500 member companies are engaged in all facets of the fresh produce industry and include growers, shippers, and wholesale and retail receivers. Collectively, the members of United handled more than eighty (80) percent of the $35 billion worth of fresh produce which is commercially marketed in the United States each year.

As purveyors of fresh commodities, our members are committed to the efficient marketing of an abundance of high quality produce at reasonable prices. The industry endeavors to supply consumers with nutritious and healthful commodities and is wholeheartedly committed to ensuring the fundamental safety of the nation's food supply.

United shares the belief which was frequently expressed during recent hearings by former and current U.S. Food and Drug Administration officials, the U.S. Department of Agriculture, numerable scientists and industry representatives that the twenty-five (25) year old Federal Food, Drug and Cosmetic Act, 21 USC §§201 et seq, has basically served this country well; however, through certain modifications the law can and should be modernized to serve the consuming public better.

Specifically, United recommends that the committee consider the following revisions in the food safety laws:

- include in the current law a statutory definition of "safe" which explicitly and unambiguously states that a zero risk standard is not to be applied by federal regulators;
- permit, under limited circumstances, the gradual phase-out of a substance with a long history of safe use for which no practical alternative exists, instead of an immediate ban which can adversely affect consumers and producers and needlessly disrupt and severely curtail the nation's food supply;
- modify the Delaney Clauses to permit the application of modern scientific advances in a risk-assessment analysis of a substance, thereby allowing a quantification of the risk and a determination of its significance, if any, to humans; and
- require federal decision-makers to submit all data to independent scientific review panels comprised of qualified experts before reaching a final agency decision about a substance.

In addition to these specific changes, United believes that certain changes in existing food safety laws should not be made. Specifically, the association supports the generally recognized as safe (GRAS) and the prior sanction provisions embodied in the current food safety laws, and any modification of these long-standing concepts is neither necessary nor advisable.

Another matter of concern to United was raised in the September 1982 draft document prepared by the Reagan administration's Subcabinet Council Working Group on Food Safety (working group). Therein, Section XIV: "Regulation of Pesticides in Raw Agricultural Commodities", proposes a change in Section 408 of the Federal Food, Drug and Cosmetic Act, supra., "to expand EPA's tolerance-setting authority to . . . provide USDA with a regulatory limit on which USDA clearly can rely . . . to inspect and pass foods with low levels of pesticide residues." (See Subcabinet Council Working Group on Food Safety document on pg. XIV-3).

Under current practices, if USDA inspectors discover a pesticide residue on an agricultural commodity, for which its use has not been approved or exempted by EPA, then USDA will generally request EPA to set a tolerance level for that pesticide on that commodity. The subsequent establishment of a formal tolerance level involves a time-consuming process, and in the meantime, USDA usually requires prompt guidance in order to approve or disapprove the distribution of the pesticide-treated agricultural commodity, especially when the commodity is a perishable one.

For instance, a USDA agent usually does not inspect a field of fresh fruits or vegetables until it is ripe for harvesting or even after it has been harvested and packed. Therefore, if a pesticide question arises, the USDA inspector needs immediate guidance from EPA or else the perishable commodity will be irreversibly damaged. Accordingly, the agencies have developed an expedited procedure whereby EPA recommends to USDA an informal tolerance level, known as an "action level", above which an agricultural chemical may be unsafe and for which USDA enforcement action should be taken. This guidance from EPA to USDA can be forthcoming within a day's time.

Despite the fact that this informal expedited procedure has worked well, the working group wishes to tamper with this process by eliminating "action levels" and substituting "interim tolerances." If the proposed change were merely semantic, United would have little concern because the current arrangement is an efficient and effective one, no matter what terms may be used to describe it. On the other hand, United believes that the establishment of a formal statutory procedure to set interim tolerances will inject into the EPA/USDA cooperative arrangement the precise element which distributors of fresh fruits and vegetables lack - time. Even a harvesting or shipping delay of a day or two can have a major impact upon fresh produce, especially highly perishable commodities, such as cherries and strawberries.

It should be noted that the change proposed by the working group is a procedural one, not a substantive one. The establishment of safe tolerance levels for pesticides on raw agricultural commodities is provided for by current law and regulatory practices. The substitution of "action levels" with "interim tolerances" will not enhance the safety of our nation's food supply. Indeed, by imposing bureaucratic delays upon the fast-paced distribution of perishable foodstuffs, such a change may ironically decrease the availability of high quality, nutritious fresh fruits and vegetables in our country's supply of food.

For these reasons the association has initial reservations about this proposal of the working group and respectfully urges the committee to proceed cautiously in this area.

In conclusion, the association commends the committee for its initiative on this important and timely issue. United looks forward to working with the committee and its staff to develop effective legislation which will continue to ensure the high degree of safety which has characterized the food supply in the United States for decades.

Statement

of the

American Industrial Health Council

Submitted in Connection with
Hearings on Food Safety Conducted

by the

Senate Labor and Human Resources Committee

June 15, 1983

The American Industrial Health Council, ("AIHC") is a broadly based diversified industry organization created to help government in the development of scientifically sound policies affecting chronic health hazards. AIHC has a membership of about 89 companies and 87 affiliated trade associations. AIHC's members produce chemicals, steel, aluminum, textiles, pharmaceutical products, forest products and a wide range of consumer goods including food products. A current membership list is attached.

Summary of AIHC Views

AIHC strongly supports the objective of improving the scientific basis for the regulation of chronic health hazards. One of the most important steps that needs to be taken at FDA and other Federal Agencies is to recognize the importance and limitations of scientific risk assessment. To determine the potential risk posed by a substance it is necessary to make an assessment of the magnitude of that risk by quantitative risk assessment techniques. Risk assessment is thus an important and necessary tool to distinguish between risks which are significant and those which are trivial or de minimus.

At the same time current methods of quantitative risk assessment have not been biologically validated and generate results which are subject to considerable uncertainty. While these defects may be remedied in the future, at the present time informed scientific judgment must be exercised in performing a scientific risk assessment to take into account biochemical and biological mechanisms, pharmacokinetics, epidemiologic data and other factors not incorporated in mathemetical models currently used to estimate human risk from animal data. To ensure the soundness of the risk assessment process and to implement the recommendations of the National Academy of Sciences and the Administrative Conference of the United States, a mechanism should be created to obtain independent peer review of the scientific data upon which food safety decisions are based. AIHC recommends that a standing Food Safety Committee be created to advise FDA on scientific matters involved in food safety regulation.

A. The Risk Assessment Process

Food safety decisions should be based on an assessment of the risk to man from exposure to a substance. The objective of FDA and USDA should not be to eliminate all risk from food - an impossible goal - but to address "significant risk" to man. While FDA has attempted to make risk assessments in the past where it believed it was permitted by law to do so, such assessments should be made in all cases where the data exists. Further, the risk assessment results should not be biased by the application of arbitrary and unscientific safety factors.

Risk assessment is the scientific process of describing the nature and often the magnitude of the risk that a defined human population will experience an increased incidence of cancer deaths as a result of exposure to a substance at stated levels for stated durations. It is a multidisciplinary function relying upon data and experience from toxicology, epidemiology, clinical medicine and experts in exposure estimation, such as industrial hygienists, demographers, and modeling experts.

It is most important that the risk assessment process begin with compilation of a valid, accurate and complete scientific data base. "Science", in this sense, comprises all the many types of data, facts, information and observations relating to the chronic health hazard phenomena. "Sound science" utilizes the data, information, etc., to the extent they are understood to be valid and utilizes the interpretations, unifying theories and judgments which are scientifically tenable.

The role of quantitative risk assessment in the risk assessment process needs to be placed in proper perspective. Mathematical modeling is an important part of the risk assessment process because typically one must extrapolate from tests using laboratory animals subjected to high doses of a substance to the much lower exposure of humans to the substance. However, it must be recognized that mathematical models at present utilize only one biological observation -- tumor incidence -- and deal only with an assumed or hypothetical dose-response function. Existing models cannot yet deal with the full range of experimental data, and the necessity of extrapolation across species raises additional problems which have not been resolved. Currently used models do not incorporate biological or pharmacokinetic information nor data on mechanism. Acordingly, risk assessment cannot be reduced to a mechanical task. A complete scientific risk assessment must include, in addition to an analysis of tumor incidence in laboratory animals, consideration of mechanism, pharmacokinetics, metabolism, positive and negative studies, tumor types and relevance to man, and epidemiologic results. At this point in its development, the risk assessment process requires the exercise of sound scientific judgment based on an analysis of all relevant data.

Finally the scientific evaluation should not include, incorporate or be limited by societal values. Judgments as to the degree of risk which should be accepted in light of a benefit of a substance are societal matters for the regulator's determination. Incorporating unreasonable safety factors or other arbitrary criteria into the scientific determination is thus an improper intrusion into the regulatory domain.

B. The Need for Independent Peer Review

The role of the regulator is to select the best regulatory response to be made, considering all factors, scientific and societal, where hazards posing significant risks are identified. The regulator should, as a risk manager, insist upon independent evaluation of all significant scientific determinations upon which he intends to rely in making regulatory and policy decisions. In particular he should obtain independent review of a risk assessment which forms the principal basis for decisionmaking concerning a substance suspected of being a chronic health hazard because of the difficulties presented in properly assessing the risks posed by such substances.

The members of this committee undoubtedly remember the great public outcry when the Food and Drug Administraion and the Department of Agriculture released a study by a researcher at MIT which implicated nitrites as carcinogenic. Nitrites have been widely used in meat products for many years to control botulism. Based on this study the two agencies began regulatory proceedings to ban or restrict the use of these chemicals. Large sums were spent by the government agencies and the meat industry on this regulatory initiative and strong public concern was raised. Careful independent review of the scientific data subsequently indicated the conclusions reached in the study were in error. The public concern was unfounded and the monies and effort expended by government and industry in starting regulatory initiatives before the review process was completed were wastefully misdirected. Because of the significance of the nitrites study it should have been subjected to careful independent review before any regulatory program was embarked upon.

The Food and Drug Administration has a very large and well developed series of advisory committees to review data on human drugs and color additives. However, scientific issues relating to food safety have not been addressed by independent science panels except on an *ad hoc* basis. There is thus no readily available means for either FDA or the regulated community to obtain an objective evaluation of the adequacy of the scientific data used for regulatory decisionmaking on food issues.

We believe that obtaining independent peer review is the single most important step in improving agency procedures to characterize risk. While the scientific review process may initially delay the regulatory process, the greater clarity of the risk estimate generated by this process will permit more precision in addressing alternatives and thus facilitate the final regulatory decision. It will also increase the confidence of industry and the general public in the validity of such decisions.

One way to ensure the highest quality scientific evaluation is to create a panel of eminently qualified independent scientists to review the scientific data and make evaluations of significant risk issues in food safety regulation. The United States has a enormous scientific resource which could be tapped for this purpose. Such a panel would assure not only excellence but greater uniformity in scientific evaluation.

Obtaining independent scientific review of the scientific data underlying regulatory decisions from a food safety science advisory committee is consistent with and would implement the recent recommendations of the Committee on the Institutional Means for Assessment of Risks to Public Health of the National Academy of Sciences ("NAS") in a report entitled "Risk Assessment in the Federal Government: Managing the Process" (March 1983) and of the Administrative Conference of the United States in "Federal Regulation of Cancer-Causing Chemicals" (June 1982). Establishment of a food safety committee also would be consistent with the Congress' creation of a scientific advisory panel under the Color Additive Amendments (21 U.S.C. § 376) and FDA's practice in the drug area.

The NAS Report

The NAS Report stresses the importance of a sound science base for regulatory decisions. Key considerations for achieving that objective are:

- maintenance of a clear conceptual distinction between the scientific assessment of risks and regulatory evaluation of alternatives of risk management;
- preparation of risk assessments providing a scientific review of all scientific data, including health data and exposure data; and
- early review by independent scientific panels of the adequacy of the data base and the validity of the scientific evaluation.

The NAS Report recommends the creation of independent science panels in regulatory agencies to provide peer review of risk assessments. It states, "Agencies and programs with mandated peer review panels . . . produce final risk assessments in support of regulatory decisions that are generally of high scientific quality and are accepted by the public and the regulated parties." NAS Report at 144. The report goes on to say that "[c]ontinuity and independence of review panels help to ensure that such panels are sensitive to regulatory needs while retaining the necessary scientific objectivity." Id. at 145. The report stresses the need for early involvement of the advisory panels in the regulatory process and recommends rotation of members for staggered, fixed terms to reduce the development of an institutional bias.

Recommendation of the Administrative Conference

The Administrative Conference of the United States ("ACUS") has also supported the need for peer review of the scientific basis of regulatory decisions. As it has stated, "Peer review of experimental findings and scientific judgments is an important means of validating the technical bases of regulatory decisions concerning carcinogens." Administrative Conference of the United States, Recommendation 82-5, "Federal Regulation of Cancer-Causing Chemicals," 47 Fed. Reg. 30701, 30712 (July 15, 1982). The ACUS has recommended that "[t]o the extent compatible with existing law, agencies should structure their decisional processes to incorporate mechanisms for scientific peer review." Id. The use of advisory panels is recommended by the Administrative Conference as one means of obtaining peer review, since

> [a]dvisory panels can contribute objectivity as well as expertise to agency decisions. Their advice has sometimes prevented erroneous regulatory actions; more frequently, their role has been to illuminate complex issues and enhance the quality and thus the credibility of agency scientific analysis. (Id.)

C. AIHC's Proposal for a Food Safety Committee

AIHC endorses the creation of a Food Safety Committee to serve as an advisory committee on scientific matters involved in food safety regulation. It is particularly important for FDA to obtain such independent peer review when the issue is the regulation of substances under the Delaney Clause.

AIHC's proposed Food Safety Committee would have the following attributes to ensure an advisory committee of high quality which will act expeditiously.

- A fixed number of members appointed for staggered terms by the FDA Commissioner from a list of independent scientists nominated by the National Academy of Sciences based solely on their scientific expertise.
- Charged with reviewing scientific data and risk assessments referred to it and submitting to the Commissioner a scientific evaluation within 120 days.
- Authorized to create subpanels composed of both committee members and outside experts and with the approval of the Commissioner, to use contractors as needed.

Conclusion

The risk assessment process should form the foundation for food safety regulations. Independent peer review of Agency risk assessments is an essential step in ensuring the validity of the scientific data which forms the basis for Agency decisionmaking on food safety. AIHC urges that the recommendations of the National Academy of Sciences and the Administrative Conference of the United States be implemented by the formation of a food safety committee composed of independent scientists.

AIHC MEMBER COMPANIES

Air Product & Chemicals, Inc.
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American Hoechst Corp.
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Dry Color Manufacturers Association
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Health Industry Manufacturers Association
Independent Petroleum Association
Institute of Industrial Launderers
International Fabricare Institute
International Institute of Synthetic Rubber Producers, Inc.
Linen Supply Association of America
Man-Made Fiber Producers Association
Metal Finishing Suppliers Association
Motor Vehicle Manufacturers Association of the U.S.
National Agricultural Chemicals Association
National Association of Manufacturers

National Association of Water Companies
National Constructors Association
National Cotton Council
National Electrical Manufacturers Association
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Wisconsin Fabricare Institute, Inc.

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The Dalles Cherry Growers
The Dalles, Oregon
JACK YOUNG
The Quaker Oats Company
Chicago, Illinois

June 9, 1983

The Honorable Orrin G. Hatch
Chairman, Labor and Human
Resources Committee
United States Senate
Washington, D. C. 20510

Dear Senator Hatch:

The American Frozen Food Institute (AFFI) is the national non-profit trade association representing frozen food processors who account for approximately 80 percent of the frozen food produced in the United States. We are pleased to have the opportunity to offer this written statement for the record documenting our views relative to the need for change in the nation's food safety laws. Indeed, we are encouraged that you and Ranking Minority Member Kennedy will be holding hearings on this issue on June 8, 9, 10. We agree, wholeheartedly, that bipartisan Congressional consideration of food safety issues is of paramount importance to the regulatory agencies, the food industry, and the American public.

AFFI's interest in this vital subject is of long-standing duration. For example, AFFI's Board of Directors, on November 10, 1981, adopted a resolution in support of the need for change of these laws as well as the principles enunciated in the legislation which you offered on June 25, 1981. (S. 1442)

I. The Need for Change

As you know, increased sophistication of analytical methodology in recent years has provided the ability to routinely detect substances at the parts per billion level and beyond. This extraordinary level of detectability, coupled with a statutory mandate embodying a "no-risk" policy for the food supply, has placed enormous burdens on the regulatory agencies charged with enforcing the nation's food safety laws. The result, oftentimes, are decisions which appear irrational to both the industry and consumers and the agencies themselves. For this reason, we concur with the National Academy of Sciences that Congress need overhaul the present food regulatory system which "has become complicated, inflexible, and inconsistent in implementation."

We believe that the existing laws should be revised in order to accommodate these advances in science and technology. In particular, we urge amending the appropriate statutes to enable the regulatory agencies to make decisions respecting the safety of the food supply in a scientifically defensible manner. This, in our opinion, dictates a movement away from the current "zero risk" philosophy. In particular, we would urge the Congress to reassess, in light of these technological and scientific advances, present requirements of the Delaney clause and the interpretation of the agencies respecting the definition of "safe." We believe that the no risk policy with respect to foods typified by, but not entirely dependent upon, the Delaney clause has raised the present concern with regard to our food safety laws. In response to this no-risk policy and the problems it has engendered, e.g. saccharin and nitrite, there have been many proposals advanced to reform the food safety laws. The common basis for these proposals is the contention that a no-risk food safety policy is unrealistic. We agree.

II. Principles for Change in the Current Law

We believe that the food safety laws need be amended to provide for a greater flexibility on the part of the agencies in making food safety assessments. In particular, such decisions must be based on a determination whether particular risks presented by a substance are so miniscule that they should not precipitate regulatory action to restrict or ban their use. For this reason, we strongly urge that Congress consider the appropriateness of adopting a concept of insignificant risks. We also recommend that food safety decisions be based upon the totality of scientific evidence. The FDA's recent inability to deal effectively with both saccharin and nitrites has made clear that the law must contain sufficient flexibility to deal with substances which may involve some risk but are, nevertheless, acceptable because of the importance of a substance to the food supply.

Moreover, because of the complexities of many of these issues, we strongly urge consideration of a statutorily mandated outside peer review to both assist the regulatory agencies in this complex decision-making process. Such a procedure will, in our view, provide consumers, industry, and the agencies with confidence in the ultimate decisions. Moreover, we believe that Congress should consider authorizing the consideration under appropriate circumstances of other factors, in addition to risk, before prohibiting or limiting the use of substances with a substantial history of use and for which there are no reasonably practical substitutes. Additionally, we believe it essential that the agencies be granted authority to gradually eliminate the use of a substance in food when such a decision would be consistent with the public interest, i.e., phaseout authority.

Lastly, we do not think it advisable to embark upon a total rewrite of the nation's food safety laws. For example, we do not believe it necessary or advisable to alter the concepts of GRAS and prior sanctions. Rather, we believe a more appropriate, as well as expeditious means of approaching the problem, would be to address the issues mentioned above. Similarly, we believe that compatible changes need be made with the food safety provisions of the statutes administered by the United States Department of Agriculture, specifically the Meat Inspection Act, the Poultry Product Inspection Act and the Egg Inspection Act.

In conclusion, AFFI strongly endorses the need for a revised statutory framework for the nation's food safety laws. We greatly appreciate this opportunity to express our views. We offer our willingness to work with you in this effort should the hearings indicate a consensus respecting the need for change.

Sincerely,

Thomas B. House
President

TBH:krg

American Chemical Society

OFFICE OF THE
PRESIDENT

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Fred Basolo
President-Elect, 1982
President, 1983
Immediate Past President, 1984

June 20, 1983

The Honorable Orrin G. Hatch
Chairman
Committee on Labor & Human Resources
U.S. Senate
Washington, D.C. 20510

Dear Senator Hatch:

The American Chemical Society strongly supports the purpose of the Delaney Clause -- to protect the American public from involuntary exposure to food additives known or expected to cause human cancer.

Unfortunately, the Clause does not permit the most appropriate use of scientific evidence in setting policy. For this reason the Society recommends that the food additive restrictions in the Clause be modified to allow the removal of the ban for any substance for which the Commissioner of the Food and Drug Administration determines the health benefit from use to be significantly greater than the risk.

At present, scientific evidence concerning the health benefits of a suspected carcinogenic food additive must be ignored in a regulatory decision. In the future, as the ability to measure extremely small amounts of chemicals increases, and as the understanding of the mechanisms and stages of chemical carcinogenesis expands, the present Delaney Clause may well force FDA to ban a product that has substantial health benefit with minimal risk to the public health.

The ACS proposes, therefore, that 21 U.S.C. 409(c)(3)(A) be changed to reflect the concept that if on the basis of appropriate tests a proposed additive is found to induce cancer in man or animal, that additive shall not be approved for use unless the available evidence demonstrates to the satisfaction of the Commissioner of FDA that the likely health benefits of such use will significantly outweigh the likely health risks from such use.

This proposed alteration of the Delaney Clause would in no way lessen the authority of the federal government to protect the public health by regulating concentrations of certain chemicals in food. The alteration would, however, permit the government to include all appropriate scientific evidence in its decision-making process.

To acquaint you better with our organization, we are including some background information. The American Chemical Society is the scientific and educational society for professionals in the chemical sciences. Founded in 1876, and granted a National Charter by Congress in 1937, the Society today has over 126,000 national and international members, representing industry, academia, government, and nonprofit institutions.

Under its National Charter, the Society is charged with the responsibility to work for the advancement of chemistry in the broadest and most liberal manner. The Society hopes that these comments on the proposed modification of the Delaney Clause of the Federal Food, Drug, and Cosmetic Act will be helpful in formulating legislation that will protect the American public from potentially harmful food additives.

Sincerely yours,

Fred Basolo

Fred Basolo

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July 1, 1983

Hon. Orrin G. Hatch, Chairman
Labor and Human Resources Committee
Dirksen Senate Office Building G-41
Washington, D.C. 20510

Re: Food Safety Law

STATEMENT OF
DR. A. KARIM AHMED, JUDITH B. KLOTZ, M.S.
AND DAVID A. WIRTH, ESQ.
OF THE NATURAL RESOURCES DEFENSE COUNCIL

Written for the Record

Dear Senator Hatch:

The Natural Resources Defense Council, Inc. ("NRDC") is a national nonprofit environmental organization supported by 40,000 members who are concerned about the health effects of chemicals, particularly in food. As part of its particular efforts to reduce exposures to carcinogenic substances, NRDC has followed the implementation of the Delaney Anticancer Clause, §§409(c)(3)(A), 512(d)(1)(H) & 706(b)(5)(B), of the Federal Food, Drug and Cosmetic Act, 21 U.S.C. §§348(c)(3)(A), 360b(d)(1)(H) & 376(b)(5)(B), with great interest.

The Delaney Clause was first enacted over twenty years ago, and since then it has served the American people well in protecting against cancer risks presented by the food they eat. Public attention has focused on the few instances in which the Delaney Clause has been invoked to bar existing additives. Perhaps even more important, however, are the untold numbers of additives that have never been introduced into the food supply -- and in many cases were never sponsored by their manufacturers for FDA approval -- because of the Clause. We believe that the scientific and policy judgments behind the Clause are as valid today as ever.

What distinguishes an additive from many other classes of potential carcinogens to which the public is exposed is, as suggested by the name, its deliberate addition to food. In the case of additives -- unlike many pollutants to which the public is involuntarily subjected -- we have complete control over exposure. The Delaney Clause is Congress's articulation of a policy not to tolerate any risk in the case of a chemical the public is deliberately exposed to. In many cases, benefits are marginal, adequate substitutes are available, or additives are unnecessary. Moreover, all color additives are strictly cosmetic at best.

Experimental evidence continues to suggest that there are no safe doses, or thresholds, for carcinogens. In other words, there are no quantities of a demonstrated carcinogen below which the risk of cancer induction entirely disappears.

The Delaney Clause has been attacked on the basis of supposedly low risks which are calculated to be associated with some weak carcinogens. When such low risks are extrapolated to the entire American population over many years, however, the number of probable cancers and the consequent degree of suffering, health expense, and loss of years of life may be substantial. Furthermore, the Delaney Clause protects the public from not one but the cumulative risks due to countless numbers of additives. The Delaney Clause is a statement that we will not tolerate such incremental risks in the case of substances over which we have complete control.

The principal benefit of the Delaney Clause is to relieve FDA of the necessity for making fine-tuned decisions in the case of every carcinogen. We believe that, in the rare instance in which a carcinogenic additive has clearly demonstrable benefits, such as nitrite, Congress should intercede on a case-by-case basis to strike a balance. Indeed, this is precisely what happened in the case of saccharin. However, as a basic principle and, in those rare cases, until Congress has had the opportunity to strike such a balance, no use of a carcinogen should be permitted. And certainly no new carcinogenic additives should enter the food supply until Congress has had the opportunity to act in this manner.

Respectfully submitted,

Karim Ahmed

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June 22, 1983

The Honorable Orrin G. Hatch
Chairman
Committee on Labor and Human Resources
U.S. Senate
4230 Dirksen Senate Office Building
Washington, D.C. 20510

Re: Federal Food Safety Policy

Dear Chairman Hatch:

The American Medical Association takes this opportunity to submit this statement for the Committee's consideration. We request that it be included in the record of the Food Safety hearings of June 8, 9 and 10, 1983.

The focus of our remarks is the "Delaney Clause" of the Food, Drug and Cosmetic Act. The "Delaney Clause" states: "That no additive shall be deemed to be safe if it is found to induce cancer when ingested by man or animal, or if it is found, after tests which are appropriate for the evaluation of the safety of food additives, to induce cancer in man or animal,...." The FDA is not authorized to weigh an additive's benefits against its health risks in making a determination to ban a cancer-inducing substance.

When the "Delaney Clause" was enacted, considerable scientific uncertainty existed concerning many issues related to the potential carcinogenicity of chemical substances used as food additives. This uncertainty led Congress to make a public policy determination that, until the scientific questions were answered, the FDA should err on the side of caution. However, even today few of the scientific uncertainties that underlie the "Delaney Clause" have been resolved: there is still no scientific consensus as to whether a threshold level exists for carcinogenisis; the significance of benign tumors observed in animal tests as an indicator of human cancer risk remains debatable; questions persist concerning the relevance of using high dosage levels in animal tests (many substances that cause cancer in animals at relatively high doses may not cause cancer in humans at the level of exposure expected with ordinary human consumption of consumer products); and, as yet, no scientific consensus exists concerning the most appropriate method for quantifying the level of human risk posed by a substance.

Because science has not yet resolved the concerns that led to the enactment of the "Delaney Clause," the appropriate basis for debate about this section of the Food, Drug and Cosmetic Act becomes whether or not the public policy judgment made by Congress represents a currently appropriate decision for our society. Thus, the appropriateness of the "Delaney Clause," or its modification, remains essentially a public policy question.

Several years ago the AMA undertook an evaluation of the food safety provisions of the Food, Drug and Cosmetic Act, focusing on the "Delaney Clause." The AMA evaluation encompassed both the scientific rules by which FDA makes a determination that an additive induces cancer in human beings or animals, and the public policy considerations surrounding continued strict enforcement of the "Delaney Clause." The evaluation resulted in adoption in December 1979 by the AMA House of Delegates of two reports by the Council on Scientific Affairs: "Food Safety and the Food, Drug and Cosmetic Act (Delaney Clause)" and "Saccharin Availability." These reports, which are enclosed, set out specific criteria for evaluating both the scientific and public policy issues surrounding continued use of a substance in the food supply. The AMA Food Safety Report concludes that: "The current Food, Drug and Cosmetic Act limits the ability of regulatory agencies to exercise judgment and thereby make comparative risk or risk/benefit assessments for food additives as a part of the decision-making process." The Report advocates amending the Food, Drug and Cosmetic Act to "require consideration of the concept of alternative risks before requiring the banning of substances suspected of being carcinogenic."

The AMA believes that the "Delaney Clause" unduly restricts the FDA's ability to utilize its best scientific judgment in establishing appropriate food safety policy because the agency is precluded from weighing an additive's benefits against its health risks. Unless the FDA is given the power to make risk-benefit assessments, the increasingly sophisticated ability of scientists to detect weak carcinogens will force the FDA to ban many additives that may present only slight risk while offering significant benefits to consumers. We advocate amending the Food, Drug and Cosmetic Act to allow for special case exemptions in the use of a food additive, despite its potential risk, if the perceived benefits from using the substance outweigh the perceived risks.

In determining whether a substance qualifies for a special case exemption, the FDA should utilize the best scientific data available concerning the usefulness, function, uniqueness, health need for, and potential risk of the substance. A special case exemption should permit marketing of the substance for only a specified time period, and require a subsequent review to take into account actual experience with the substance. In addition, the FDA may need to make marketing approval of a substance conditional or restrictive, in order to protect the population as a whole or a specific population sub-group.

The American Medical Association commends the Committee for its inquiry and stands ready to assist in developing suitable legislation to restructure the federal law on this important subject.

Sincerely,

James H. Sammons, M.D.

JHS/dap
0933p

Statement of the
AMERICAN PUBLIC HEALTH ASSOCIATION
on
The State of Our Food Safety Laws

The American Public Health Association is gratified for this opportunity to offer our public health perspective to this national dialogue on our food safety laws.

As an organization that represents over 50,000 health professionals in every aspect of community and public health, The American Public Health Association is deeply committed to health promotion and disease prevention for the welfare of our citizens.

Since Upton Sinclair and Harvey Wiley mobilized Americans to the need for government safeguards to protect the purity and wholesomeness of our food supply, Americans have enjoyed one of the world's safest food supplies built on and assured by strong food safety laws.

The Federal Food, Drug and Cosmetic Act has been a bulwark for nearly five decades since its inception against encroachments on the healthfulness of our food supply. Legislative and administrative refinement of this landmark law has kept it tuned to changing nuances in our food system. Even judicial interpretations, such as Monsanto v. Kennedy, 613 F.2d 947 (1979), have reaffirmed the continuing wisdom of this law.

Our food safety laws were enacted to protect the health of the public. As the organization that represents professionals singularly dedicated to this same goal, the American Public Health Association urges the Congress to rededicate itself to the original intent of our food safety laws, the protection of the public's health. This renewed commitment to food safety means strengthening the law, where necessary, and rejecting suggestions to eviscerate our food safety laws.

The law could be strengthened in several ways. All components of our food supply, including prior-sanctioned foods, should be tested for safety. The Congressional intent of the Color Additive Amendments of 1960 should not be thwarted by the provisional listing of additives in perpetuity. Testing of food additives should be broadened to include tests for their drug-nutrient interactions and their possible effects on behavior.

Attempts to erode our food safety laws such as suggestions to change the definition of what is "safe" and to reverse the intent of the Delaney Clause should be vigorously opposed. Similarly, risk assessment methodology is neither sufficiently sophisticated nor proven to warrant its premature injection into food safety decisions.

The American Public Health Association is on record as a strong supporter of our current food safety system. Any alterations should be reforms that strengthen the law and renew its vigor for safeguarding the health of the public food supply.

Submitted Statement

to the

U.S. Senate
Committee on Labor and Human Resources

Food Safety Oversight Hearings
June 8-10, 1983

Paul R. Thomas, M.S., R.D.
Public Health Nutritionist

Senator Hatch and members of the Committee, I thank you for allowing this statement to be incorporated into the hearing record.

I am Paul R. Thomas, a nutrition educator, a registered dietitian, and presently a doctoral student in the Department of Nutrition Education, Teachers College, Columbia University. Before coming to New York City, I served as a public health nutritionist with the Monongalia County Health Department in Morgantown, West Virginia, and in my last year there formed a Division of Nutrition Services which I then administered. For two years I was also an adjunct instructor in the Department of Community Medicine at the West Virginia University School of Medicine. At Teachers College, I have worked as a staff nutritionist at their Nutrition Education Resources Project.

Through these positions I have taught nutrition to a wide variety of audiences, from very young children to medical students and residents, and to adults in the general population and in clinic settings. As a nutrition educator, it is my responsibility to translate the findings of nutrition science in a form understandable to my audience, and to provide practical information on developing appropriate dietary patterns and food selection skills. In addition, I translate governmental food policy statements so that individuals may know how such policies will affect their food choices, how they will work to simplify or make it more difficult to eat nutritiously, and either help contribute to feelings of security or unease in the ability of our present food supply to nourish us.

I provide these comments as a nutrition educator, not as a research nutritionist, nutritional biochemist or a food technologist. They reflect my fears that if present food safety laws are altered, it may well be in a direction that, to my way of thinking, will weaken them. I will focus on how I believe such changes will affect my job as an educator, as well as how I think the general public will view the safety of their food if undesirable changes in the laws are enacted.

Food safety law is not a topic commonly taught in the training of nutritionists. Much of what I know comes from reading government documents, as well as books and articles on the subject. It certainly is a difficult area, and there are many sources of confusion for me. Peter Barton Hutt, former chief counsel at the Food and Drug Administration (FDA), speaking about food law, stated, "I would say there aren't more than five people in the country who really understand it." I'm likely to agree. Mr. Hutt is one of those five, and I wish he were closer to my side of the issue. He is a lawyer with numerous food industry clients, including the Grocery Manufacturers of America.

As a nutrition educator, it is difficult for me to teach the historical development of food safety legislation without giving the student the impression that it is a patchwork of policies administered by several agencies that invites differential treatment of food constituents with comparable risks. The present law is complicated and inconsistent in implementation. That impression is not one providing confidence that the foods we eat are safe.

Food Safety Laws

The Food, Drug and Cosmetic (FD&C) Act of 1906 was the first federal statute governing food safety. A food would be considered adulterated if it contained "any poisonous or other added deleterious ingredient which may render such article injurious to health." Only added food substances were addressed by this legislation. In 1938 Congress rewrote the law, expanding provisions in the 1906 Act. An adulterated food is defined by Section 402 as one that "bears or contains any poisonous or deleterious substance which may render it injurious to health..." This section also dealt with indigenous food substances by stating, "...in case the substance is not an added substance such food shall not be considered adulterated under this clause if the quantity of such substance in such food does not ordinarily render it injurious to health." This standard dealing with potentially poisonous substances in food has remained unchanged. A toxicant such as nitrites in spinach will be considered to adulterate the food only if it "ordinarily render[s] it injurious to health." I believe this is as it should be. Most, if not all, foods contain substances which can be considered hazardous by themselves at some level. We know very little about how such substances interact with the other components in food to either weaken or potentiate toxic effects. Many of these foods, however, contain levels of nutrients which make them valuable to us. The fact that toxicants may be present in our foods (usually at very small levels) should make us wary of adding additional ones to our foods intentionally.

In Section 406 of the 1938 Act, the FDA was empowered to establish tolerances for "added" toxicants whose occurrence in food cannot be avoided, or whose use is "necessary" to produce the food. Pesticides on raw agricultural commodities are an example of this type of toxicant, although I question whether pesticides, at least in the amounts we use many of them today, are "necessary" to produce various foods. This law did not precisely define words such as "unavoidable" and "necessary."

Several amendments have been added to the 1938 Act to deal with sub-categories in the class of "added" food substances. The first was the Pesticide Residues Amendment of 1954, now section 408 of the Act. It states that a raw agricultural commodity will be considered adulterated if it bears any residue of a pesticide not conforming to a tolerance established under this section. An elaborate procedure was described by which the FDA established such a tolerance. The Environmental Protection Agency (EPA) now establishes these tolerances; I do not know whether it does so in collaboration with FDA.

Congress enacted the Food Additives Amendment in 1958. An adulterated food could now be considered as one containing a food additive not approved by FDA in a food additive regulation, or one that contained an approved food additive in quantities exceeding the legal limit specified by FDA. This law applies to substances intended for addition to formulated foods, as well as substances that become or "can reasonably be expected to become" components of food, such as packaging materials. There are two important exceptions to the coverage provided by this amendment. Hundreds of additives are designated as GRAS (generally recognized as safe) so are legally not considered food additives. This list includes items such as sugar and salt, as well as a substance like dilauryl thiodipropionate. Secondly, substances that were either FDA or United States Department of Agriculture (USDA) sanctioned for use in food prior to 1958 were also not legally considered food additives (the so-called "grandfather clause.") (It is difficult to explain to an audience that food additives considered GRAS or prior sanctioned are not legally "food additives" without causing confusion.)

In 1960 Congress passed the Color Additives Amendment, dealing with substances used to color foods, as well as drugs, cosmetics and medical devices. A food is considered adulterated under this amendment if it contains a color additive whose use in food has not been approved by the FDA, or whose use exceeds the amounts permitted by FDA regulations.

The most recent modification to the 1938 FD&C Act was the Animal Drug Amendments of 1968. Under section 512 of this Act, no animal drug likely to leave residues in edible tissues of livestock may be used, nor may foods containing such residues be marketed, without FDA approval.

Built into the Food Additives, Color Additives and Animal Drug Amendments is the so-called Delaney clause, which states simply (in language easy to understand!):

> No additive shall be deemed to be safe if it is found to induce cancer when ingested by man or animals, or if it is found, after tests which are appropriate for the evaluation of the safety of food additives, to induce cancer in man or animal...

This clause obviously generates much debate and controversy among all contestants in the food safety debate. I will discuss this issue in some depth later in my statement.

At no point has Congress specifically addressed the problem of environmental contaminants which find their way into food, such as PCBs or mercury. Therefore, FDA has classified these contaminants as "added poisonous or deleterious substances" whose occurrence in food cannot be avoided, in order to bring into play its tolerance setting authority under section 406.

The net effect of the Food, Drug and Cosmetic Act and its subsequent amendments have been to treat substances in our food in one of two ways. Substances defined as food additives, color additives and animal drugs are embodied in the law's "no risk policy" which prohibits their use in food if there is any reasonable indication that they may induce cancer in humans or animals. Other substances, such as pesticides and environmental contaminants, may continue to be used on foods under sections 406 and 408 of the Act which allows the FDA to set tolerances, even though scientific studies may indicate a reasonable chance they induce cancer in humans or animals. Therefore, the FDA has sharply contrasting approaches to dealing with substances in food such as saccharin and the pesticide 2,4,5-trichloroethylene. Many desire changes in food safety laws, but differ radically on the type of changes to be made. One camp, in which I am a member, argues that the food safety laws should be strengthened, so that the Delaney clause will be applied to all substanced added to food, as well as modified so as to invoke the law in regard to diseases in addition to cancer. The other camp argues that the Delaney clause is too absolute, and does not allow for risk-benefit calculations to be made in deciding the fate of added food substances. They would like to see it dropped or modified to permit the FDA to look at benefits as well as risks in deciding whether to ban such a substance.

Now I would like to comment on specific issues in the controversy over food safety.

Safety

In fiscal year 1978, the latest year for which I have figures, the Department of Health, Education and Welfare (now DHHS) spent $81 million on food safety. Most of the responsibility rested with the Bureau of Foods within the FDA. An additional unknown sum of money was spent by USDA to try to insure the safety of meat and poultry products. Presumably this includes the testing of food chemicals, evaluation of manufacturer's data on additives and animal drugs, and law enforcement activities such as seizures and recalls of adulterated foods.

The fact is that it is impossible to have a food supply that is totally and truly safe. By its very nature, a food system presents hazards to consumers in the form of natural constituents in the foods, deliberately added substances, incidental additives and environmental contaminants. The policy objective needs to be the management of risk by minimizing it as best as current knowledge allows. A nutrition educator must make this clear to the public.

The FD&C Act does not define the word "safe," although it insists that food additives, color additives and animal drugs be "safe" prior to sale to the public. The law, however, does establish some criteria for determining safety. These include probable consumption levels, accumulated effects of components of the additive and related substances in the diet, and safety factors used to apply animal test data to humans. The law does not otherwise require or prohibit FDA assessment of the health, economic or other benefits of the proposed additive, except in those cases where the Delaney clause may apply. I find it amazing that only as late as 1958 were these three categories of food chemicals mandated to be proven safe before being allowed in foods. Prior to that time, additives were allowed in foods until the government could "prove" in a court of law that they were hazardous to health. Even now, some color additives (Red #3 and Blue #2, for example), on which few safety tests have been conducted, are found in foods, and evidence exists to cast some doubt on their safety. The FDA has defined safety as "a reasonable certainty in the minds of competent scientists that [a chemical additive] will not be harmful to the public under its proposed conditions of use." It is the best that can be done right now to define something as safe if there appears to be no apparent risk associated with it, with the understanding that this could change based on future research.

I would oppose any change in the definition of the word "safe" to mean, for example, "the absence of significant risk under the intended conditions of use." This is too ambiguous a definition:

- Under this definition, a 1/1,000,000 risk could be deemed "not significant" since any individual's risk is small, but could still be significant in terms of the number of people in the country at risk.
- It is unclear whether FDA could take into account cumulative exposures. The risk to a consumer exposed to 100 chemicals, each with a 1/1,000,000 risk, would be 1/10,000, and this cumulative exposure could lead to problems in 20,000 individuals in the country.

The Delaney clause

Probably no other part of the entire food safety laws has created as much heated debate as the Delaney clause. It has become a symbol to every interest group wanting to influence the laws. Those who desire to strengthen food safety laws generally praise the clause, while those wanting to "weaken" them belittle it.

It might be considered redundant to have the Delaney clause (which prohibits cancer causing additives and animal drugs in foods) in the food safety laws when other sections already state that a food additive can be approved only if found safe for its intended use. However, in the report on its evaluation of saccharin and food policy issues in general, the National Academy of Sciences noted that the Delaney clause was a unique addition to the law, because:

- the existence of a strongly worded anti-cancer provision may make regulators and courts extremely wary of suspected or possible carcinogens,
- it may deter industry from manufacturing and proposing new additives that not only are subject to costly and time-consuming experiments, but also must meet a difficult statutory test,
- the clause prohibits carcinogenic food additives regardless of the level of risk, and
- the clause explicitly states that known animal carcinogens as well as known human carcinogens, are unacceptable as additives.

Judging by the amount of debate, one might think the Delaney clause responsible for removing many additives from the food supply. In fact, in the 25 years that this law has been on the books, only two additives have been banned because of it, Flectol-H in 1967 and chroanaline in 1969, both components of food packaging adhesives. Only two of the 12 additives banned between 1959 and 1977 were due directly to Delaney. Most of the others were banned by the general safety provisions of the FD&C Act.

Those who desire to modify or remove the Delaney clause from food safety laws state that as more substances are tested for carcinogenicity, more of them will be found to be carcinogenic in at least some test animals. In addition, the advances in analytical chemistry have allowed us to detect traces of additives in the parts per trillion range, so that any carcinogenic food additive would have to be banned even if discovered in very small, "insignificant" amounts. They also argue that as the number of epidemiological studies multiply, more and more substances will be suspect carcinogens.

I believe, along with numerous others, that the logic of Delaney is just as sound now as it was back in 1958. Since there are no known threshholds for inducing cancer, we should be very wary of introducing chemicals into our food supply as intentional additives if there is any hint of cancer-causing potential. Contrary to popular belief, the Delaney clause does require the use of scientific judgement in deciding the results of experiments. Delaney would not apply to substances found to be carcinogenic only in inappropriate or inadequately conducted animal experiments, or are otherwise indicated to be carcinogenic only in experiments with results that scientists generally deem inconclusive. Substances are not banned, as some critics have facetiously complained, "at the drop of a rat."

Also contrary to popular belief, everything does not cause cancer if fed in large enough amounts to some animals. Back in 1969 the National Cancer Institute tested 120 pesticides and industrial chemicals thought to be carcinogenic by feeding them to animals in doses as large as could be tolerated. Only 11 of them gave any proof of being carcinogenic. Therefore, it would be fair to assume that the percentage of any 120 randomly selected chemicals found to be carcinogenic would be far less.

The Delaney clause is in trouble today because it threatens the availability of saccharin, the only available artificial sweetener, and for a time threatened to remove sodium nitrate and nitrite from processed meat products. Neither of these substances have acceptable substitutes and are widely used in food products, so there is understandable resistance on the part of the food industry and many consumers to have them banned. Saccharin has been shown to be at least a weak carcinogen. Nitrates and nitrites do not appear to be carcinogens, but the nitrites can combine with secondary amines found in many foods to form nitrosanimes, a potent class of carcinogens. In addition, nitrates can be converted directly into nitrites.

It is my belief that the so-called inflexibility of the food safety laws--their inability to take into account the supposed benefits of saccharin--is no reason to mount major efforts to "reform" (I read that word as "weaken") those laws. I feel it is primarily a political matter to decide whether the benefits of a food additive outweigh any proven or suspected risks to overrule a ban. Congress has decided to postpone a ban on saccharin, overruling the decision FDA had to make based on considerations related to the Delaney clause. (This may have been an entirely appropriate action, depending on whether the vote accurately reflected public sentiment, or resulted from the extensive lobbying of industry groups.) If as a society we want to assume some risk from a substance, we must make that decision through our elected representatives. I don't believe it should be the FDA's role to generally make risk-benefit calculations.

Risk Assessment

Some supporters of changes in food safety laws argue that regulatory bodies such as FDA should conduct risk assessments, calculating some benefit-risk ratio to determine whether a food additive shown to carry some risk if consumed should still be allowed in foods. Risk assessment seeks to weigh the health consequences of exposing citizens to some risk against the perceived benefits derived from taking the same action. It sounds simple and desirable to calculate risk-benefit ratios, but in fact the risks and benefits are almost impossible to measure objectively.

Edward Groth III of Consumers Union has made a list of the information necessary to make good policy decisions about the risks and benefits of a substance:

1. What is the substance?
   Physical and chemical properties.
   How does it get into food? (Natural constituent, additive, environmental contaminant, etc.)

2. Human exposures
   Exposure levels for specific human populations.
   Range of exposures; groups with high exposures.
   Which foods contribute to exposure?
   Is food the only source? If not, how do other sources of exposure compare with dietary intake?
3. Uptake, metabolism, pahrmacokinetics
   Absorption from foods (in humans).
   Metabolic and anatomic fate in the body (where it goes, and is it transformed?)
   What levels (doses) are present at sites of potential biological effects?
4. Biological effects
   Biochemical and physiological mechanisms of action.
   Nature of effects: Organs and systems affected; timing of effects (acute, chronic); consequences for health and functioning of the organism.
   Dose-effect and dose-response relationships.
   What degree of biological change is detrimental?
   Any beneficial effects? (Essential nutrients, etc.)
5. Factors that affect toxicity
   Host variables (age, sex, reproductive status).
   Biological interactions (with nutrients, medication, pathogens, etc.)
   Physical factors (temperature, radiation, etc.)
6. Population-specific risk assessments
   Quantitative risk estimates for:
   general population
   subpopulations with high exposures
   subpopulations with inherent high susceptibility; infants, pregnant women, others.
7. Opportunities to reduce risks
   Nature of interventions (safer alternatives, contamination control, warning labels, etc.)
   Effectiveness of alternatives at reducing risk.
   Cost and feasibility of alternative approaches.
8. Function and benefits of the substance
   Why is it present in foods? (Intentional additives)
   Are there alternatives with the same function?
   What benefits could be lost if action is taken to reduce risks?

Groth then makes a very important statement:

> Ideally, we would hope that decision makers would be able to collect and analyze reliable scientific data on each of the topics listed. The decision step, then, would require value judgements. Scientific assessments can aim to say what risks are associated with exposures, and what costs and benefits are likely to follow from measures intended to reduce exposures. Regulatory policymakers still must make subjective judgements to determine how much risk is socially acceptable, or what cost is reasonable to attain an acceptable level of risk.

In fact, very few substances have reliable scientific data available on each of the topic areas described by Groth to make value judgements. Sanford Miller, Director of FDA's Bureau of Foods, expresses pessimism that good risk-benefit ratios can be determined for most additives:

> A rigorous risk/benefit ratio is intrinsically impossible with our present knowledge of food additives. The term calls for dividing a very uncertain probability of risk in an ill-defined series of controversially adverse physiological responses in undefined units, by a heterogeneous collection of so-called benefits, such as economic gains expressed in dollars, convenience expressed in yet-to-be-agreed-upon measures, aesthetic appeal not expressible in numbers of any kind, and so on.

Clearly, Dr. Miller would not like to be in the business of making risk assessments.

The Food Safety Council, a coalition of industry representatives, lawyers, economists, a few consumer advocates and others, feels that risk-benefit ratios need to be calculated for substances in food, and have provided a number of suggestions to that end. Still, much work needs to be done, and it is obvious that the quantification of risks and benefits will be based on few hard facts. In the case of saccharin, for example, the National Academy of Sciences found that the risk of cancer varied five millionfold--from 0.0007 cases to 3,640 cases per 50 million people exposed to saccharin--depending on the risk assessment model which was used. In addition, NAS found no studies which permitted an objective assessment of the benefits of saccharin. There is no proof that saccharin is effective in attaining and maintaining desirable weight. There are no economic benefits to consumers, for diet soda is just as expensive as sugar containing soda. Even though saccharin is one of the most widely studied food additives, it seems to me that there is not enough information to calculate a meaningful risk-benefit ratio.

I tend to agree with journalist Greg Moyer of the Center for Science in the Public Interest, who concludes that if the Delaney clause is altered to allow risk assessment investigations, "FDA rulemaking would be cut adrift in a sea of subjectivity." He calls risk assessment a "pseudoscience." Risk is usually borne by consumers while benefits accrue to the food industry in the case of most additives. When I ask the question "How much social benefit is derived from the additive that produces the risk?" the answer is usually "none." Is it that important that we have new added chemicals in our food supply to make cornflakes in various colors, or chocolate cake taste more "chocolate," without chocolate? Not according to the people I talk to.

Public Perceptions

Sidney Wolfe of the Health Research Group has noted that the consumer, as well as the producer and the regulator of risk, must be involved in determining whether chemicals should be added to food. Generally the consumer is worried about these substances. As the Congressional Research Service has noted:

> Several sources have suggested that while the public

> is aware and willing to take certain other risks in life, they are not willing to consume risky food additives or related constituents. This perception exists because food is taken for nourishment and enjoys an intimate relationship to health so that consumers expect more care to be exercised than is taken in other areas of life.

The General Accounting Office in 1981 found 12 public opinion polls over the previous ten years addressing issues of food safety. Generally they showed that the public supports the Delaney clause, that cancer causing food additives should be banned. However, people were generally opposed to a ban for substances such as saccharin which have perceived benefits and have been in use for a long period of time. In my experience, I have also noted that the general public is wary about chemicals in their food, but can be very supportive of saccharin, which they associate with diet foods and drinks where a choice exists either to use them or their sugar containing counterparts. It seems to me that any changes in food safety laws mandating risk-benefit assessments for carcinogens to be added to foods goes against the will of a majority of the public.

Some individuals argue that the public should have available food products which contain substances that pose a certain level of risk and let them decide individually whether benefits outweigh the risks to them. However, as Washington lawyer Harrison Wellford points out, "when you talk about freedom of choice, you've got to be sure that both parts of that term apply." There is really no choice involved if the person is a fetus, a child, illiterate, educationally disadvantaged, or even a customer in a restaurant. There is also no choice if the information provided is not adequate to make the distinction between alternatives.

The National Academy of Sciences has noted that there are many difficulties in providing information to the public:

- it is not easy to convey warnings about small and ambiguous risks. There is difficulty in conceptualizing small-probability hazards, and abstract statistical information is much less compelling than concrete information,
- the scientific basis for assuming the presence of food risks is often subtle, and vulnerable to public skepticism (for example, animal studies use very large doses of a substance under investigation),
- there is a danger the public is satiated with health danger warnings, and would pay little attention to any given warning because of an increasing perception that "everything causes cancer," and
- public trust in actions of government appears to have declined over the past ten years, and a lack of credibility of government-sponsored information may limit its effectiveness.

I conclude from this that the public interest is served by tough food safety laws which take a hard line against substances shown to cause cancer in appropriate experiments, but are flexible enough to allow people to vote, through their representatives, when they feel a particular risky substance should stay on the market. Such voting would not occur often. The present food safety laws now on the books allow this to be done for many substances in our food.

Conclusions

As a nutrition educator, I am constantly providing information to individuals on selecting foods to insure a nutritious diet. Basically that means eating wholesome, minimally-processed, natural products: fresh or lightly cooked fruits and vegetables; whole grain breads, cereals and pastas; legumes; nuts and seeds; eggs; fresh lean meat, fish and poultry products; low-fat dairy products--cheeses, yogurts and milk. When I answer the many questions consumers have about food additives and how to minimize their intake of them, I again suggest they eat wholesome, minimally-processed natural products.

These wholesome foods as a group contain few additives. Most additives occur in what are commonly called junk foods, foods that are relatively low in vitamins, minerals and protein while containing fairly large amounts of sugar, salt and/or fat. Most nutritionists advise that we eat as few of these foods as possible.

My greatest reservation about food additives relates not to their safety or lack thereof, but to the fact that they make it possible to produce such a variety of enticing convenience food products that often compete with time-tested nutritious foods. Too often, these wholesome foods lose out to the taste, convenience and advertised appeal of formulated foods, and resultant nutritional problems can occur in the long run. It is only with additives that these new food products can be made.

Too many of the products now on supermarket shelves undermine my nutrition education efforts. First of all, with up to 15,000 items in an average supermarket, it becomes more difficult to choose from among them to insure a nutritious diet. Secondly, the variety of formulated foods available makes it difficult to provide guidelines in proper food selection. For example, Sugar Smacks cereal shares a greater similarity to candy than to cereal, but is considered a cereal, in the same category as hot oatmeal and Shredded Wheat which are superior products. Tang, containing no fruit juice, is often wrongly considered equivalent to orange juice. Hot dogs are seen as equivalent to fish, both belonging to the "meat" group. And so on. I believe the consumer would be better off with fewer foods to choose from, and where educational efforts would concentrate on demonstrating the ease, taste appeal and general convenience of preparing and using naturally nutritious foods. Then the safety question of many additives would become a moot one; there would be no reason for them in the food supply. I realize this is not a realistic scenario at the present time, given an economic system in which food companies profit most from producing formulated, brand-name food products.

I think it is overall a healthy attitude that we view novel, added chemicals in our food supply with suspicion, and the present FD&C Act for the past 77 years has attempted to protect Americans from poorly tested and dangerous additives, especially those that might be carcinogenic. To the best of our knowledge, there is no safe dose of a carcinogen, and we are unable to determine a given individual's sensitivity to a carcinogen.

Risk assessment of additives has nowhere near the sophistication yet of providing a reasonable determination of benefits and risks; both are impossible to quantify unarguably in most cases.

I think that food safety laws need to be strengthened, not weakened. Several loopholes need to be closed:

- as of now, additives in use prior to 1958 are virtually exempt from food safety laws. They should be tested in accordance with contemporary standards,
- testing of color additives, which have remained on a "provisional list" for more than twenty years, needs to be expedited,
- food additive testing should be broadened to include testing their effects on behavior and the central nervous system, and there should be tests for interactions between commonly used additives, drugs, alcohol and other food ingredients. Testing should be carried out on each additive at regular intervals, to take advantage of further refinements, sensitivities and improvements in procedures.

I realize that a general lack of agreement among sides makes any attempted changes in the present food safety laws a difficult challenge. I am made uneasy by the fact that even members of the National Academy of Sciences panel studying food safety policy issues could not come to agreement on the characteristics of such a policy. While the majority thought that a food safety policy should discriminate among risk levels of additives and assign priorities among categories of risks, allowing variety in regulatory approaches, a minority disagreed. They argued that additives cannot be classified into various risk categories using current data and theories, and desired a food safety policy that involved little agency discretion. When it comes to chemicals in our environment (especially those added to our food) and considerations of public health, it is evident that there are many unanswered questions, and disagreement with one another's value judgements is the rule rather than the exception.

Most importantly, the philosophy of the original Food, Drug and Cosmetic Act should be maintained, that chemicals should be proven safe prior to their introduction in food. I believe we should be as careful as possible in changing our food safety laws and err on the side of caution, and most people I have taught agree with my assessment.

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REFERENCES

Center for Study of Responsive Law. Eating Clean: Food Safety and the Chemical Harvest (readings). Washington, D.C.: Center for Study of Responsive Law., c1982.

Comptroller General of the United States. Regulation of Cancer-Causing Food Additives--Time For a Change? Washington, D.C.: General Accounting Office, December 11, 1981.

Focus on Food Safety. Proceedings of the 4th National Food Policy Conference. Day 1--Tuesday, April 7. Washington, D.C.: Community Nutrition Institute and Food Marketing Institute, c1981. Day 2--Wednesday, April 8.

Food Safety Council. Principles and Processes for Making Food Safety Decisions. Food Technology, March 1980 (Supplement).

Hartman, S., D. Porter, E. Withnell. Food Safety Policy Issues. Congressional Research Service Report No. 81-155, June, 1981.

Hatch, Senator Orrin, for himself and others. Introduction of a bill S.1442, to amend the Federal Food, Drug and Cosmetic Act, the Poultry Products Inspection Act, the Federal Meat Inspection Act, and the Egg Products Inspection Act to improve food safety decisions, etc. Congressional Record, Thursday, June 25, 1981.

Martin, James G. The Risk/Benefit Regulation. An Occasional Paper from the Institute of Nutrition, University of North Carolina, March 19, 1979.

National Academy of Sciences-National Research Council Committee for a Study on Saccharine and Food Safety Policy. Food Safety Policy--Scientific and Societal Considerations. Part 2 of a two-part study, March 1979.

Office of Technology Assessment. Environmental Contaminants in Food. Washington, D.C.: U.S. Congress Office of Technology Assessment, December 1979.

Senator Orrin G. Hatch
Senate Committee on Labor and Human Resources
4232 Dirksen Senate Office Building
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Dear Senator Hatch:

We would like to submit for your consideration our views on food safety legislation. We respectfully request that this letter be included in the record of the Senate Committee on Labor and Human Resources' recent hearing on this matter (June 8-10, 1983).

1. Delaney amendment: The Delaney amendment is a clear enunciation of the public's desire to minimize the risk of human cancer due to food (and color) additives and is a crucial element in our society's efforts to prevent cancer. While it is impossible to totally protect the public from cancer-causing agents in food, the Delaney amendment provides excellent protection from cancer-promoting substances added intentionally to foods. Everything possible should be done to prevent cancer, a disease that kills over 400,000 Americans every year and whose incidence is rising.

The Delaney amendment is an important scientific statement that recognizes that (a) there is no threshhold level below which a carcinogen does not increase the risk of cancer, and (b) data derived from well-conducted animal studies are as valid as human studies. A wide range of public and private expert committees over the past two decades have endorsed the scientific basis of the Delaney amendment. We know of no new evidence that would cause these concepts to be revised.

Over the past quarter-century the Delaney amendment has functioned well. Because few food additives have posed a cancer risk, the amendment has been invoked only rarely. Furthermore, just once in 25 years, in the case of saccharin, have political considerations pre-empted Delaney and caused Congress to make an exception to the law. It is unlikely that many cancer-causing additives like saccharin will arise in the future, because there is much redundancy among food additives and for most functions several alternative additives are available. Repealing the Delaney amendment would send a strong signal to the public that this Congress is not concerned about preventing cancer.

2. Risk assessment: Researchers are developing mathematical models to estimate the risk that a chemical may pose to humans. Risk assessments can sometimes be useful in providing rough estimates of a chemical's risk and for setting priorities. However, it is currently (and for the foreseeable future) impossible to make accurate assessments of a chemical's carcinogenic threat to humans on the basis of animal studies.

There are three basic unknowns that even the most sophisticated mathematical model cannot account for: (a) animals may be much more or much less sensitive to the carcinogenic or other property of a chemical; (b) the human population is extremely diverse in terms of genetic make-up, especially compared to highly inbred animals used in cancer tests, and it is likely that some individuals will be far more susceptible to harm caused by a chemical than others; (c) humans are exposed to a myriad of drugs, pollutants, and other agents from which test animals are protected and with which the additive might interact to potentiate the risk of cancer. The existence of these confounding, unpredictable factors prevent accurate risk assessments from being made. When a National Academy of Sciences committee reviewed the safety of saccharin, it found that different models for risk assessment gave estimates that spanned a 5-million fold range, from 0.0007 to 3640 cases of bladder cancer per 50 million people. Legislation should not endorse or require the use of an inherently unreliable technique by mandating that the FDA ascertain and prohibit only so-called "significant" risks.

3. Risk-Benefit: As difficult as it is to do a risk assessment, it is even more perilous to do risk-benefit analyses of food (or color) additives. Because virtually all additives serve only a cosmetic purpose, rather than a health benefit, dangerous additives should be banned. Putative economic benefits to restricted segments of society should not be allowed to counter-balance health risks to the public. This usually poses no problem to either the public or the food industry, because there are generally several additives available that can substitute for one another in a given food.

In rare circumstances, an additive that is both unique and serving a health purpose may be discovered to pose a risk, though we know of no such additives currently in the food supply. In such instances, it would be appropriate to do a risk/risk assessment to help compare the harm caused by the additive to the harm that might be caused if the additive were banned. However, making an accurate assessment is most difficult. For instance, in the case of sodium nitrite (which some parties claim provides a health benefit that no other additive or process can provide), the data were inadequate to estimate with any accuracy either the amount of cancer that nitrite may be causing or the amount of botulism that the absence of nitrite might result in.

For this reason, we caution the Committee against including requirements for risk-benefit analysis in any proposed food safety legislation. Congress can act on a case by case basis in rare situations in which an otherwise dangerous additive should remain in foods because it is irreplaceable and provides a countervailing health benefit.

4. Phase-outs: When a food (or color) additive is discovered to be harmful, it should be banned immediately. This ordinarily does not pose a problem to industry, because FDA's procedures and the public debate provide food companies with adequate time -- several years in most cases -- to switch to another substance. Only in the unusual case in which an additive is unique and beneficial to the public health should phase-outs even be considered, and, in those cases, the phase-out period should be strictly defined and limited.

We appreciate your considering our views.

Sincerely,

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STATEMENT FOR THE RECORD
FOOD SAFETY HEARINGS
JUNE 8-10, 1983
CONDUCTED BY
COMMITTEE ON LABOR AND HUMAN RESOURCES
UNITED STATES SENATE

SUBMITTED BY
JOHN G. MOHAY
PRESIDENT
NATIONAL MEAT ASSOCIATION
WASHINGTON, D.C.

JUNE 23, 1983

NATIONAL MEAT ASSOCIATION STATEMENT FOR HEARING RECORD
FOOD SAFETY HEARINGS, JUNE 8-10, 1983
COMMITTEE ON LABOR AND HUMAN RESOURCES
UNITED STATES SENATE

If consumers are to receive the full benefits of the food supply, the nation's food safety laws must be modernized. Otherwise, in all likelihood, many beneficial substances eventually will have to be removed from the food supply. The archaic laws that currently regulate food have not kept pace with the rapid advances in technology. Today, scientists routinely detect substances in parts per trillion; this figure was unheard of in 1958 when the food laws were last rewritten.

The preponderance of evidence and foresighted scientific and regulatory thinking agree the changes should be made now. The debate begins when the discussion shifts to who will lead the effort. Controversy surrounds this issue. But, until Congress acts, a threat of impending disaster will continue to hang over the food industry and consumers.

The National Meat Association, which represents many of the nation's most successful meat packers and/or processors located throughout the nation, has intimately experienced the chaos that the current laws can create.

In 1978, Dr. Paul Newberne (Massachusetts Institute of Technology) rocked the meat industry and alarmed consumers nationwide when he linked the nitrite used to cure meat products to cancer in rats. Had the letter of the law been applied, nitrite would have been banned and the public denied the protection it provides against botulism--a deadly food poisoning.

As it was, nitrite became a serious question mark in consumers' minds. Each time they ate a cured meat product they had to consciously weigh the publicized health threat it supposedly presented against the nutritional and sensory benefits the product provided. Needless to say, consumers were caused immeasurable concern and the meat industry lost untold millions of dollars in sales because of a false alarm.

And that is exactly what it was, a false alarm. Sounded prematurely. Only after the public had been loudly warned that nitrite caused the world's most frightening disease, and countless consumers had switched their dietary habits to omit cured meat products, did an independent group of pathologists prove that Dr. Newberne had based his findings on faulty science.

Congress owes it to the American public to do whatever is necessary to assure that a mistake of this magnitude and cost does not happen again.

The National Meat Association believes now, while the food supply is between crises, industry, the administration, Congress and the scientific community should proceed with deliberate haste.

A crisis atmosphere does not produce clear, rational thinking or results. Unfortunately, however, it is only during panic situations that the public clamors for action.

This association is convinced Congress must lead the reform effort. Otherwise, nothing fruitful will happen. We are encouraged by these hearings. They have demonstrated the unanimity that exists for updating our food safety laws. The record generated by this hearing has laid a solid foundation. This committee now must take the next step: Initiate legislation that will build on this foundation.

Whenever a major undertaking is contemplated, there is always a hesitation to begin. Perhaps the complexity of the issue makes it hard to find a starting point. Fortunately, with food safety, a logical beginning exists: The Delaney Clause.

Although the Delaney Clause is only a small part of the total Food, Drug and Cosmetic (FD&C) Act, it carries the potential to effectively devastate our entire food supply. The meat industry learned this lesson well when the U.S. Department of Agriculture and the Food and Drug Administration in 1978 announced a plan to phase out nitrite.

Specifically, the Delaney Clause generates these problems:

1. It does not recognize the tremendous advances that have been made in food measurement techniques since being added to the FD&C Act in 1958. There have been

three generations of new measuring instruments since 1979.

Food analyzed in 1958 and considered safe might be banned if analyzed by today's intricate equipment. Scientists routinely detect quantities of suspect carcinogens that are a million times smaller than was possible in 1958. Traces of these substances, however, are impossible to remove by any known manufacturing process.

2. Its "zero-risk" requirement prohibits weighing benefits against risks for a suspected carcinogen.

Scientists do not know if a threshold for carcinogens exists. Perhaps there is a level of exposure below which cancer will not result. X-rays, in excessive amounts, can cause cancer but we use them because of the tremendous benefits they provide.

The Delaney Clause, had it been invoked, would have prevented the public from weighing nitrite's protection from botulism against the risk of cancer because of the "zero-risk" mandate. Yet, a FDA risk assessment issued in June 1978 estimated "22 deaths would occur from botulism in the first year after-total removal of nitrite from cured meats unless an intensive educational program was instituted."[1] The same study said only six cases of cancer would occur yearly that could be "attributed to nitrite in cured meat."

3. It deals only with substances added to food. It does not deal with all food chemicals which might be carcinogenic and found naturally in food.

4. It assumes that animal experiments are accurate predictors. It assumes that high doses of substances fed to experimental animals accurately predict the effect of small doses in humans.

   Aflatoxins fed to animals in a given amount could cause 1 million to 10 million times as many cases of cancer as the same amount of saccharin. These vast differences in the degree of risk must be taken into account in setting regulatory policy.

Many definitions for "safe" have been suggested. We believe the key to a successful definition lies with Congress. Lawmakers must define safe and quantify what is an "acceptable risk." The regulatory agencies must have a target area to work within. The more precisely acceptable risk is defined, the more sense our food safety laws will make and the more effectively they can be administered.

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[1] General Accounting Office, "Does Nitrite Cause Cancer? Concerns About Validity of FDA-Sponsored Study Delay Answer," January 1980, p. 31.

The National Meat Association also recommends that peer review be an integral part of setting policy to regulate the food supply. In the academic community, peer review has been used for years to assure that published research is correct and reflects the "state of the art." Regulatory decisions of a scientific nature could benefit from the same procedures in the food safety area.

Had peer review been required in 1978 and Newberne's findings double-checked prior to being made public, the nitrite scare and resulting confusion and monetary losses would have been avoided.

SUMMARY

The National Meat Association strongly supports efforts to modernize the laws that govern the nation's food supply. The association recognizes that the current law has provided Americans with the world's most wholesome and safest food supply. But, at the same time, we also recognize that the giant strides made in food technology have left an ever-widening gap between the laws that determine food policy and scientific capabilities that force regulators to act--not always in the best interest of the public. Couple this situation with the totally rigid Delaney Clause and it is inevitable that future confrontations, such as the nitrite fiasco, will erupt.

To spare consumers from these chaotic episodes that confuse them and leave them distrustful of both the food supply and the government's ability to protect them, we recommend this committee start the reform movement by developing legislation that will bring about the needed changes.

The time to begin is now while the country is between food crises. This is an ideal opportunity to proceed unemotionally and with common sense.

The National Meat Association pledges its help in bringing the nation's food safety laws in line with today's technology.

Thank you.

The CHAIRMAN. With that, we will adjourn these hearings.

[Whereupon, at 1:15 p.m., the committee adjourned.]

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